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DISEASES OF THE VULVA

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THE vulva is regarded as including the labia majora and minora, mons veneris, clitoris, perineum and its folds, Bartholin's glands and the vestibulum vaginae. The meatus urinarius and hymen, although not entirely vulvar in origin, are often considered as a part of the vulva because of their close relation to other vulvar structures.

The external surface of the labia majora is covered with the skin. The inner aspect of the labia majora, the labia minora and clitoris present more the appearance of mucous membrane, but they are in reality covered by a modified epidermis or true skin. In this particular these structures may be compared to the lips, which are midway between mucosa and skin.

Various forms of dermatosis may, therefore, affect the vulva as other portions of the skin, i.e., psoriasis, lichen planus, eczema of different types, pemphigus and impetigo. Eczema may be due to general constitutional causes or to local infections, as in other parts of the body. It is probably most frequently due to the presence of an irritating vaginal discharge. Savill (1929) notes also that eczema marginatum of the vulva due to Epidermophyton inguinale has been more recently observed in England since the War.

As a result of rape or traumatism, the relaxed tissues of the vulva may suffer the formation of a very large hematoma.

MYCOTIC INFECTIONS

The vulva is also subject to mycotic infections, most frequent of which are those due to monilia. These infections are frequently associated with pregnancy.

Mycotic infections of the vulva have been classified by Le Blaye as follows:

Creamy vulvitis, resembling oral thrush in appearance, with a white thick exudate covering a mucosa that is inflamed but not ulcerative; usually associated with similar lesions in the vagina (creamy vaginitis).

Ulcerative vulvitis: a severe form with superficial ulcerations, pain, lymphangitis, and enlargement of the inguinal glands.

Pseudoleucoplakic vulvitis: The mucosa appears whitish and opaque, as in leucoplakia; by curettage the whitish coat can be removed with the superficial layer of the mucosa, but the tissues underneath do not show the characteristic wrinkling or true keratinization of leucoplakia.

Eczematiform vulvitis, without exudate; there is formation of vesicular pustules, which rupture and form small punctiform erosions.

Pruritus without inflammatory reaction and only a few erosions due to scratching; it may be of long duration and is not accompanied by lichenification or atrophy of the mucosa.

Vesiculopustular cutaneous forms, affecting only the skin of the vulva and surrounding areas; the vesiculopustules are

small, the vesicular stage of short duration, and healing rapid.

In all these types of mycotic vulvitis, the diagnosis depends upon the demonstration of the organism in the lesions.

Popoff, Ford, and Calmus have recently (1929) reported a mycotic vulvovaginitis, occurring in a woman during the latter part of pregnancy, in which the first symptom was pruritus of the vulva accompanied by a discharge, at first thin and later thicker and somewhat cheesy and granular. There were lumps of white exudate on the vulva and in the lower vagina, which could be removed by gentle rubbing with gauze. Underneath this exudate the mucosa was inflamed, but there were no ulcerations or bleeding points. From this exudate the monilia of thrush was isolated.

Tuberculosis of the vulva is of rare occurrence, but various forms of lupus have been described.

VULVAR ULCERS

Previous to the work of Lipschütz, various authors had described the occurrence of small acute ulcers on the vulva, sometimes associated with aphthae in the mouth. Lipschütz found numerous thick Gram-positive bacteria in the smears from these ulcers, but at first was not successful in obtaining pure cultures. Later he was able to isolate this bacillus in pure culture with the use of ascites-agar. But, in the meantime, Scherber had isolated this organism in pure culture anaerobically. To this organism Lipschütz gave the name of Bacillus crassus. Ulcus vulvae acutum is of comparatively rare occurrence, only about 60 cases having been reported.

Lipschütz distinguishes three types of acute ulcer of the vulva.

1. The gangrenous form with ulcers developing suddenly on the outer genitalia, associated with burning pain, fever and chills. These ulcers sometimes perforate the labium minus.

2. The venereal form with ulcers at the labia minora and in the vagina. The ulcers are sharply defined, not so deep as in the previous type, very painful to the touch, and not accompanied by fever.

3. The miliary type, with numerous small ulcers not larger than a pin head always occurring in combination with the second type. Bacillus crassus is always found in the smear in almost pure culture. While usually multiple, single ulcers may occur (one case reported by Carol and Ruys). The bacillus belongs to group of organisms that form lactic acid and very closely resembles, if it is not identical with, Doederlein's bacillus, normally found in the vagina. Finnerud is of the opinion that various factors lowering the local tissue resistance render this saprophytic organism pathogenic for the vulvar tissues.

SYPHILOMA VULVAE

Chronic ulcer of the vulva with secondary elephantiasis was frequently reported in early literature under the name of esthiomène. In this condition the anus was also involved. Heimann and I reported such a case in 1912. The lesions in this case, when the patient came under observation, involved an area extending from the mons veneris over the labia majora backward to about an inch behind the anus and laterally about 2 inches to either side of the intergluteal fold and over the glutei. All the lesions were hard and not tender. Over the mons and the labia there were macules, papules and cysts. There was some superficial ulceration of the lesions, but not of a characteristic type. In this case there was no evidence of syphilis or tuberculosis, but a probable gonorrheal infection with rectal stricture.

In 1920, I reported 2 cases with similar lesions; but, from a study of the history and pathology of these cases and a review of the literature, I came to the conclusion that this type of chronic ulcer of the vulva, formerly known as esthiomène, is a manifestation of tertiary lues and pathologically shows changes characteristic of gumma. In 1925, a new case was reported further supporting these conclusions. The lesion is characteristically a slowly progres-

sive indurated tumor causing no pain, but some inconvenience on account of its size. The vulvar tissues are swollen and indurated and usually the site of deep-seated ulcers, which show no predilection for any particular site. This combination of hypertrophy and ulceration, it is to be noted, is characteristic of syphilis.

Fig. 1. A. Syphiloma vulvae (after Stein and Heimann).

Histologically, a syphiloma consists of a collection of round cells closely resembling the cells derived from inflammatory neoplasms with scanty blood vessels. The affected tissues, like all gummata, undergo processes of necrosis and cicatrization with contraction of scar tissue. According to Lubarsch, gummatous nodules are microscopically interpreted as granulating inflammatory products which are especially rich in lymphocytes and frequently show fibroblasts and fibrillary tissue. The products pass either into solid connective tissue or undergo necrosis in the area of the cellular as well as fibrous portions, the original general tissue structure often remaining recognizable in the form of

Fig. 1. B. Syphiloma vulvae (after Stein).

fibrous strands, traces of blood vessels, and cells without nuclei. Whereas small syphilomata in their earliest stages resemble condylomata and contain chiefly small inflammatory cells as well as plasma cells, those which have attained a large size possess a more variegated structure, containing plasma and epithelioid cells besides small round cells of lymphocytic type and presenting diffuse extensive caseation often surrounded by small nodules containing epithelioid and giant cells. These structures are liable to be confused with those of tuberculosis, the following features being of value for the differential diagnosis: In syphiloma the epithelioid cells are usually less numerous than the small granulation and plasma cells. Fibroblasts and fibrillar connective tissue are apt to be conspicuously represented in syphiloma but are only exceptionally demonstrable in tubercles. Caseation is more extensive, as a rule, in syphilomata than in tubercles and, in the former, occurs in the stage of connective-tissue transformation, whereas in

tubercles caseation invariably precedes this change. As a result, a caseated syphilitic focus usually still contains demonstrable tissue elements, whereas a caseated tubercle forms an amorphous mass. In a general way, the diseased tissue presents hypertrophic and inflammatory changes. The microscope shows an accumulation of embryonic cells in the middle layer of the dermis arranged around the blood vessels and progressively diminishing in frequency at a distance from the vessel. The lymphatics are dilated and packed with endothelial cells. The subdermic tissue likewise contains a large quantity of dilated vessels. These lesions terminate in the formation of scar tissue and sclerosis.

Fig. 2. Syphiloma vulvae.

While the essentially syphilitic nature of the so-called esthiomène is not acknowledged by all authorities, there is an increasing tendency to accept the conclusion that it is at least indirectly due to syphilis even in cases where syphilis is not demonstrable, developing on a soil prepared and altered by syphilis. Kehrer is of this opinion, although he believes other factors are necessary for the production of esthiomène. His conclusions from a review of the subject are that the several factors involved are:

First, an injury to the tissues, especially the smaller arterial vessels due to a previous syphilitic infection. Secondly, a dilatation and stasis in the veins due chiefly to sexual disturbances and excesses.

Fig. 3. Elephantiasis of vulva and lower extremities (after Kehrer).

Thirdly, a functional blocking of the regional lymph glands due to inflammation or their surgical removal. Fourthly, an ulceration on the tissues thus predisposed due to any bacillary infection, but chiefly to the tubercle bacilli; of secondary importance are gonococci, streptococci, staphylococci or Ducrey's bacillus. The rare occurrence of this condition is due to the fact that so many factors are needed for its production.

CHRONIC ULCER AND ELEPHANTIASIS

Recently Joachimovits has described a form of chronic ulcer of the vulva with elephantiasis observed in the tropics. He saw 17 cases of this type in two months in Java. It occurs also in India, but in some parts of India is very rare. The vulvar lesion is usually, but not always, accompanied by a rectal stricture. Most of these cases were not seen until the ulceration was in a chronic stage and the vulva showed elephantiasis. If actual elephantiasis has not developed, the labia majora are edematous and hard. The labia minora are usually atrophied.

Some of these patients had demonstrable syphilis but Joachimovits found no evidence that the vulvar lesion itself is of a syphilitic nature. The spirochetes of syphilis were not found. The histologic changes were not characteristic of syphilis and arsphenamine treatment was without effect. The lesion found was a fusospirochetosis due to a symbiotic infection with spirochetes and fusiform bacilli.

CHRONIC HEMORRHAGIC VULVITIS

In 1921, Lipschütz described a form of chronic vulvitis ("chronic hemorrhagic vulvitis"), reporting 4 cases. Of these patients one had syphilis and one gonorrhea. In the other 2 cases there was no evidence of venereal disease. One had pulmonary tuberculosis. In 3 of the 4 cases there was severe anemia, due in one case to syphilis; in another to tuberculosis, and in the third to no definitely demonstrable cause. The lesions were yellowish red spots with uneven edges on various parts of the vulva. Histologic examination showed chronic inflammatory changes with hemorrhagic infarcts. They were painless and did not cause pruritus.

In 1928, Karyschewa reported another case of this type. His patient had both syphilis and gonorrhea. The appearance of the vulvar lesions corresponded to that described by Lipschütz; the patient was definitely anemic. The lesions were painful on urination, but otherwise caused no symptoms. This case is the fifth of this type reported.

PAGET'S DISEASE OF THE VULVA

In 1929, Drake and Whitfield reported a case of Paget's disease of the vulva. The diseased area was a "lurid red." Both labia majora were involved and the disease extended into the groin farther on the left side than on the right. Both labia were swollen and edematous. The exterior surface was moist and desquamating. There was fissuring at the anterior margin of the vulva and in the folds of the groins. The inner surfaces of the labia had the "red velvet" appearance similar to that seen in Paget's disease of the breast with numerous small areas of white epithelium. Histologic study of a dropsy specimen showed typical Paget cells, especially in the basal layer of the epidermis, the hair follicles and sweat glands. Drake and Whitfield found only 4 other cases of Paget's disease of the vulva reported in literature.

PRIMARY VENEREAL MANIFESTATIONS

In addition to syphiloma vulvae, the primary lesion of syphilis (the typical chancre) may develop on the vulva. The inguinal glands are always enlarged, sometimes on the same side as the vulvar lesion, sometimes on the opposite side, and sometimes on both sides. Diagnosis is made by the demonstration of the Spirocheta pallida in the lesion.

Soft chancre or *ulcus molle* may also occur on the vulva. The lesions are often multiple.

In adult women a gonorrheal lesion is sometimes found on the vulva, usually in the region of Bartholin's glands; but, aside from the gonorrheal vulvovaginitis of children, gonorrheal lesions rarely involve the vulva.

GRANULOMA INGUINALE

Venereal granuloma, ulcerating granuloma of the pudenda, or granuloma inguinale, when it occurs in women, usually involves the vulva. The disease occurs chiefly in tropical and subtropical countries, but in recent years a number of cases have been reported in the United States, occurring chiefly in negroes. In women the ulceration usually originates in the labia minora and extends to involve other vulvar tissues, the vagina, the tissues around the anus and the inguinal region. The so-called Donovan bodies first described in 1905 are now regarded as the etiologic agent in granuloma inguinale and they can be demonstrated in the lesions in practically every case. Tartar emetic given intravenously has proved the most effective treatment for this condition.

Among 18 cases of granuloma inguinale reported from Bellevue Hospital by Campbell in 1927, only 2 occurred in women; in both the labia were involved. In one of these cases there were small lesions about the lower labial angle with a moderate-sized granulomatous ulceration in the lower vagina. A similar lesion had been excised six months previously, but there had been a prompt recurrence. The lesion at that time was thought to be an epithelioma, but histologic examination showed it to be a granuloma. In both cases, the lesions healed rapidly under treatment with tartar emetic. Campbell stated that the disease begins as a small moist papule, which ulcerates rapidly and invades the surrounding tissues with a reddish granulomatous proliferation, ulcerating superficially when moist. The lesions, when moist, as is usually the case, are covered with a thick mucoid exudate that has a "peculiar stench, somewhat like dead fish." The lesions are only "mildly sensitive" and the patients do not complain of pain.

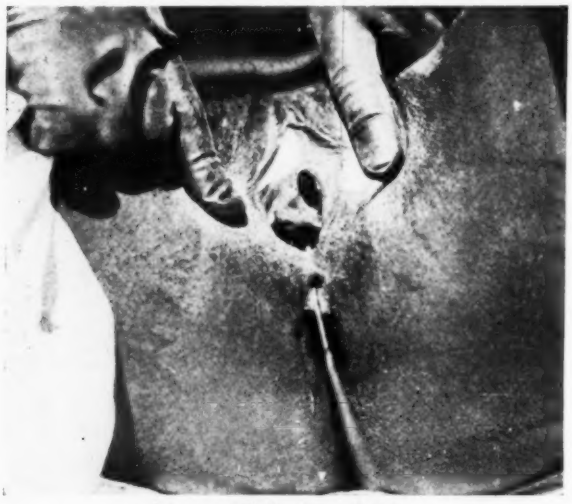

Fig. 4. Diabetic vulvitis.

PRURITUS VULVAE AND DIABETIC VULVITIS

Pruritus vulvae may be a symptom of many diseases of the vulva. It may be a very annoying symptom with no lesion except reddening and some edema of the parts. Scratching causes excoriation and, as the affection persists, the skin becomes white and thick. Pruritus is a very common symptom in women with diabetes. In these cases, as a rule, if treatment is not instituted early, an erosive eczematous eruption develops. While local treatment should not be neglected, the control of the diabetes is the most essential factor in the treatment. For the local treatment of pruritus of the vulva, I have long advocated cleansing of the parts with oil and the application of an ointment (lanolin base) containing cocaine, menthol and salicylic acid. Aqueous and alcoholic solutions should not be used.

LEUCOPLAKIA AND KRAUROSIS VULVAE

One of the most interesting lesions of the vulva, and one that has been the subject of much discussion, is leucoplakia, or leucoplakic vulvitis (Taussig) and its relation to kraurosis and cancer. Leucoplakia is an inflammatory condition characterized by the formation of whitish plaques, composed of thickened epidermis. Kraurosis is characterized by atrophy of the tissues. The relation of these two conditions is still a matter of discussion, but the more recent contributions to the literature indicate that kraurosis is a later stage of leucoplakia. Thus Kehrer regards it as established that kraurosis shows two stages: a hypertrophic hyperplastic stage, always associated with leucoplakia, and a later atrophic stage. Terruhn states that there may be leucoplakia without kraurosis, but kraurosis does not occur without leucoplakia.

Graves and Smith, in a recent study of 18 cases of kraurosis vulvae, found both leucoplakia and kraurosis in every specimen. In leucoplakia the epithelium is chiefly involved and especially the squamous epithelium, showing hypertrophy and keratinization. In kraurosis the derma is chiefly involved with the most marked atrophic changes in the corium. Graves and Smith found that in leucoplakia the papillae were enlarged and thickened and extended into the corium, while the corium was somewhat denser than normal, but much less so than in kraurosis.

In 1929, Taussig reported 40 cases of leucoplakic vulvitis. Twenty-eight of these 40 patients showed a symmetrical involvement of the entire non-hairy portion of the vulvar skin from the mons veneris to the margins of the anal ring, and occasionally around the ring; in 22 cases kraurosis was present. In 30 cases the leucoplakia had developed after the menopause; in the other 10 cases, there was some abnormality of the menstrual function.

Taussig is of the opinion that the underlying cause of leucoplakic vulvitis is a loss of elasticity in the skin due partly to deficiency in the ovarian hormones. Terruhn also believes that leucoplakia and kraurosis are due to ovarian dysfunction which brings about trophic disturbances in the vulva through the sympathetic nervous system. Taussig advocates vulvectomy, more or less complete according to the location of the lesions, as the only effective treatment of leucoplakia. Of 23 of his cases in which this operation was done, 2 patients died, one postoperatively, and 4 could not be traced. Of the 17 patients traced, 16 were cured, 9 of them for over five years. A severe pruritus is usually an early symptom of leucoplakia, but Terruhn and others note that not all patients show this symptom.

BENIGN TUMORS

In rare cases fibromyomas may rise from the vaginal wall and protrude from the vulvar orifice.

Fibrosarcoma of the vulva and labia is rare. Only one case was seen by me and operated upon. A diagnosis of cyst of the labium had been made and at operation three small, hard, round solid tumors were removed, which, according to the pathological findings were typical fibrosarcomas. The pathology reported is as follows: Sections of the tumors show elongated fusiform cells which are often arranged in slender bundles which frequently interlace or form whorls. Some of these cells are slender, while others are plump. The nuclei are for the most part rod shaped with rounded ends, simulating the nuclei of smooth muscle cells. The bundles

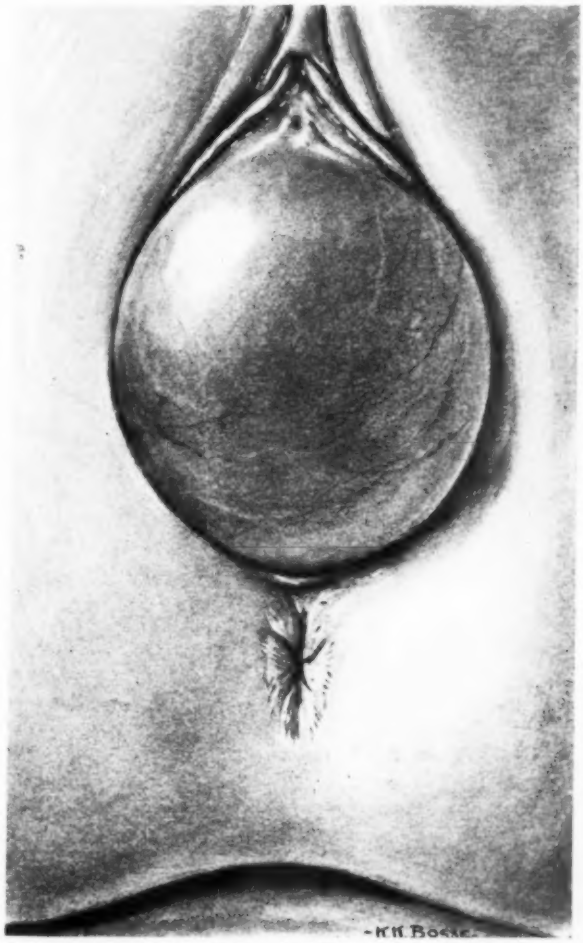

Fig. 5. Fibromyoma of vaginal wall protruding through vulvar orifice (after Stein).

are supported by a varying amount of fibrous tissue which is for the most part acellular and prone to hyaline degeneration. The tumors are fairly well supplied with blood vessels and show areas of edema. Mitotic figures are not observed, and nerve fibers are not demonstrable. Scattered through the growths are a few small collections of small round cells.

The vulva may be the site of benign or malignant tumors. Fibromata of the vulva usually originate in the subcutaneous connective tissue. They consist chiefly of connective tissue elements, but usually contain some muscle fibers. In a few cases these tumors arise from the extra-abdom-

inal portion of the round ligament of the uterus. Brady in 1929 reported a case of the latter type. He stated that less than

Fig. 6. Pedunculated fibroma of labium minus with primary luetic lesion of vulva.

175 cases of fibromata of the vulva have been reported in literature. In his case the tumor contained an epithelial inclusion cyst, a tube lined with several layers of squamous layer of epithelium. This is a unique finding in a vulvar fibroma. Cases of lipoma, myxoma, papilloma, and sweat gland tumors or hidradenoma of the vulva have also been reported, as well as cases of benign cystic tumors. The latter are usually retention cysts, such as retention cysts of Bartholin's gland and sebaceous cysts. Recent reports of such benign tumors include a case of hidradenoma reported by Blau in 1928, and a case of lymphatic cyst reported by Lunsford and Schauffer in 1929.

In Blau's case of hidradenoma, the tumor developed on the left labium major as a small nodule. There was a small opening at the top. When this opening was enlarged with a scalpel, there was no discharge of pus, but a small piece of tissue projected into the opening resembling lipoma tissue. Histologic examination showed it to be an adenoma of a sweat

Fig. 7. Large cyst of labium majus.

gland. There was no evidence of malignancy in this case, yet the irregular and atypical proliferation of the epithelium suggested the possibility of malignant degeneration. This has also been noted in other cases of this type reported. Blau found 12 other cases reported in the literature without definite signs of malignancy, and 2 additional cases in which there were definite carcinomatous changes.

In Lunsford's and Schauffer's case, the cyst developed on the left labium minus. These authors note that lymphatic cysts of the vulva are rare. They found only 5 other cases reported in literature involving the labia minora and in only one of these was the growth limited to the labia, as in their own case.

In 1927, Henry reported a case of an endometrial growth on the right labium majus. This was first noted as a small hard nodule three years prior to admission to the hospital. It had gradually increased in size and shortly before admission a second nodule had developed near the first. The nodules were tender at all times, but

became swollen and painful at the time of menstruation. The mass was removed without difficulty and showed no infiltration of the surrounding tissue. The operation was done two days before the expected menstrual period. The tumor contained one large cyst and several smaller cysts. It was found to be an adenofibroma containing uterine glands and stroma. Similar growths have been reported as adenomyomata. Henry believes that this growth was due to transplantation of endometrial cells into the tissues of the labium majus as a result of injuries during childbirth or their vascular (lymphatic or venous) dissemination, more probably the latter.

SARCOMA OF THE VULVA

Of malignant tumors of the vulva, sarcoma is rare but extremely malignant. The pigmented variety (melanosarcoma) is the most malignant, metastasizing early and tending to recur rapidly after operation. Sarcoma of the vulva may occur in girls under twenty. In 2 recent cases, reported by Netzer in 1925 and Morgan in 1928, the patients were seventeen and sixteen years of age respectively.

In Netzer's case the tumor was on the right labium minus and the inguinal glands on that side were enlarged and hard when the patient was first seen. The tumor was excised with a considerable margin of normal tissue. The tumor site and the lymph gland area were given two series of roentgen-ray treatments; but, in spite of this, there was an early recurrence, from which the patient died within eight months after the operation. Netzer concludes that deep roentgen-ray therapy cannot be depended upon to improve results in sarcoma of the vulva. He notes that sarcoma of the vulva may resemble fibroma clinically, and exact diagnosis is possible only by histologic examination in some instances. Diffuse infiltration of neighboring tissues, immobility of the tumor and reddening of the skin over it indicate sarcoma.

In Morgan's case the tumor was a rapidly growing, unpigmented, round-cell sarcoma. While the growth had been noted less than two months before admission to the hospital, the inguinal glands were already enlarged, indicating that metastasis had taken place. The tumor was fixed in position and very painful. Radon seeds were placed in the tumor with resultant diminution in the size of the growth and relief of pain. In the meantime metastases had developed in the right ilium and pubic bone. A series of roentgen-ray treatments was given, but the patient failed rapidly after leaving the hospital. Morgan is of the opinion that in cases of vulvar sarcoma seen very early, radical excision with deep *x*-ray treatment would be the treatment of choice; but, if metastasis has taken place, excision is not indicated. Radium is probably best for palliative treatment. He notes that all growths about the vulva, especially fibroma and hard tumors in the region of Bartholin's glands, should be removed early to guard against sarcomatous degeneration.

Fig. 8. Sarcoma of vulva.

CARCINOMA OF THE VULVA

Carcinoma of the vulva is more frequent and of more clinical importance than sarcoma, although rare in comparison with the frequency of carcinoma in the internal genital organs. Cancer of the vulva is of an extremely malignant type, although it occurs as a rule in older women.

The point of predilection for the origin of primary carcinoma of the vulva, judging from a comparative study of the reported cases, is in the labia majora and minora as well as the clitoris. Beginning as a small hard nodule or thickening of the tissue, the growth extends from its starting-point to the clitoris, urethra, and external genitals, which finally become transformed into an amorphous tumor mass, although even in advanced stages the primary tumor in the vulva remains localized to a certain extent and recognizable as such. In the course of the extensive suppuration which follows, the large secondary cancers which have developed in the inguinal glands are liable to become infected and break down.

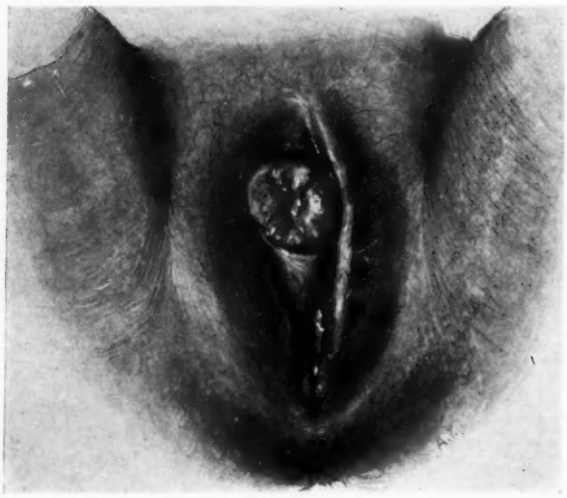

Fig. 9. Primary carcinoma of vulva.

Metastases are limited, as a rule, to the regional as well as lumbar lymphatics, the glands in the groin being usually involved as well, whereas the iliac and hypogastric glands are less frequently affected. Involvement of the adjacent skin and mucosa of the external genitals results in so-called "contact" cancer, the *Abklatsch-Krebs* of German writers. The neighboring hollow viscera are directly invaded by the primary growth in a number of cases. In its continued development the cancer encroaches upon the pelvic connective tissue, especially the rectovaginal and vesicovaginal septum. The pelvic bones, more particularly the descending pubic ramus, may next become diseased and carcinomatous.

Especial importance is attached to the early involvement of the regional lymphatics, the external inguinal glands representing the first stage, the deep inguinal glands the second stage, the external iliac, hypogastric, and obturator glands the third stage of cancerous invasion.

Fig. 10. Primary carcinoma of vulva.

The necessity of radical surgical treatment with removal of the inguinal glands is emphasized by most recent authors. Radium and the roentgen rays are also employed in the treatment of vulvar carcinoma, but are of value, as far as recent reports indicate, chiefly as an adjunct to surgery.

De Büben, however, has recently reported a series of 31 cases of cancer of the vulva treated at the First Gynecological Clinic of the University of Budapest with radium and the roentgen rays alone. Most of the patients were over sixty years of age. The majority of the growths were squamous cell epitheliomata arising in the labia majora or minora. Radium was employed for treatment of the local growth, usually by the use of small radium tubes embedded in the tumor, and the roentgen rays were used for irradiation of the lymph glands. Of the 31 cases treated during 1918 to 1928, 2 patients are living and free from recurrence for six years after treatment; 4

others are living and under observation; the other patients have died, the longest survival period being four years.

Voltz also reports 31 cases from the Gynecological Clinic of the University of Munich treated by radiation. Of these, 4 patients were living without recurrence five years after treatment. In a review of the literature, he found 57 cases of vulvar carcinoma reported that were treated by radiation alone, with 7, or 12.2 per cent, of five-year cures.

Schreiner, however, reports from the New York State Institute for the Study of Malignant Disease at Buffalo, New York, that there was no five-year cure of cancer of the vulva obtained at that institution by the use of radiation alone (radium and the *x*-ray). He has found the best results to be obtained by electrocoagulation of the tumor combined with high voltage *x*-rays over the lymph gland areas and the implantation of gold radium seeds into metastases or recurrences.

Recent reports by Taussig and from the Mayo Clinic (Rentschler) indicate the value of bilateral lymphatic dissection as increasing the percentage of five-year cures.

Of the 76 cases reported by Taussig, a fairly definite classification could be made in 67 cases. Of these 51 were of the epidermal type arising from the labial perineal or preputial skin; 2 were true carcinoma of the clitoris; 10 were vestibular carcinoma; and 4 were Bartholin gland tumors. In 6 of the cases no treatment was attempted; 21 cases were treated with radium, the *x*-ray, or both; and 49 patients were operated upon by vulvectomy, which in 18 cases was combined with a superficial or incomplete gland removal and in 16 cases with double, complete gland removal (Basset operation). In most cases radium or the *x*-ray failed to produce even a temporary amelioration of symptoms. No cures were obtained in any of the 15 cases treated by this method that were traced. Of the cases in which simple vulvectomy were done, 6 patients had been operated upon five years earlier and none had survived the five-year period. Of 13 cases traced in which a partial gland removal had been done, 4, or 30 per cent, were free from recurrence after more than five years. Of 11 cases in which vulvectomy with complete gland removal had been done, 9, or 81 per cent, were free from recurrence, one at five and a half and the other at eight years. Seven were living and well at the time of the report.

In Rentschler's report of 71 cases of primary epithelioma of the vulva from the Mayo Clinic, the youngest patient was twenty-seven years of age, the only one under 30; the oldest was eighty-six years of age; the majority were in the sixth and seventh decades of life. In 34 of the cases the lesion was ulcerating when the patient was first examined. There were 30 cases in which the inguinal lymph nodes were enlarged; 9 of these were regarded as inoperable; in 3 others the nodes were not removed at the time of operation; in 18 cases the nodes were removed at the first operation and carcinoma was demonstrated histologically in these nodes in 14 cases. The inguinal lymph nodes were also removed in 15 other cases at operation, although they were not palpably enlarged. Carcinoma was found in these nodes in only 3 instances. In all these cases the primary growth was definitely on the vulva, originating most frequently in one of the labia majora. There was a prominent tumor without ulceration in 37 cases, and in 34 cases ulceration with or without tumefaction. Microscopic study of the growth was made in every case; in the 2 cases of Bartholin gland tumor it was an adenocarcinoma; in all other cases squamous cell epithelioma. According to Broders' classification, there were only 3 cases of grade I, but 45 cases of grade II, 17 cases of grade III, and 6 cases of grade IV. The grade II cases approached grade III more nearly than grade I. Of the entire series of 71 cases, 3 patients died following operation; 6 could not be traced, of whom 4 had lymphatic involvement at the time of

operation; 45 have died, all but one of carcinoma (but 7 of these lived five years or longer); 13 are living without recurrence, 9 of them five years or over and 2 fifteen years; 4 are living with recurrence (in 2 of these cases the recurrence took place after the five-year period). Of 15 patients operated upon by extirpation of the growth and bilateral lymphatic dissection, 4 are living and free from recurrence; one had recurrence only after eight years.

Rentschler is of the opinion that in cancer of the vulva wide excision of the local growth with excision of the superficial and deep inguinal nodes on both sides, whether enlarged or not, supplemented by radium and roentgen-ray, is the treatment of choice, unless metastases have developed or the malignancy is of grades III or IV. In malignancy of grades III or IV, excision of the local growth followed by radium and the roentgen rays over the site of the local growth and the lymphatic drainage is preferable.

PRECANCEROUS LESIONS

Recent studies have indicated the importance of leucoplakia as a "precancerous" lesion of the vulva. Taussig found a coexisting leucoplakia in 39 of his 76 cases of carcinoma. In 21 cases of cancer of the vulva in which a histologic examination was made by Graves and Smith, leucoplakia was found in 16 specimens and kraurosis in 14 of these. In cases in which leucoplakia and kraurosis were not found, either the carcinoma was far advanced or the tissue specimens were not satisfactory. In all but 2 instances in which leucoplakia was found, the matrix of the cancer was definitely leucoplakic; in 2 cases the cancer was closely associated with a true kraurosis and may have developed from kraurotic tissue. This indicates the need for vulvectomy in cases in which permanent leucoplakic or kraurotic changes have developed.

Of occasional interest with regard to the vulva are the atypical male ensembles sometimes observed in connection with pseudohermaphroditism.

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VALUE OF THE ROENTGEN RAY IN GYNECOLOGY

(EIGHTH COMMUNICATION)

ADDITIONAL STUDIES OF THE CORNUAL SPHINCTER, THE PHYSIOLOGIC CONTRACTION AND RELAXATION OF UTERINE COMPONENTS, AND THE SPECIAL USE OF SMALL QUANTITIES OF OPAQUE MEDIA*

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NEW YORK

ROENTGENOGRAPHY, more than any method except laparotomy, offers the most precise aid in the revision of doubtful pelvic findings. It also helps to form an accurate diagnosis in cases where the history, symptoms, and bimanual palpation have led only to speculative interpretations of the true condition. In the selection of therapeutic measures appropriate to any given cases, roentgen examination performed with the addition of the various contrast media is often of the greatest value. When the type of operation is in question, a uterogram will influence the surgeon's decision as to whether myomectomy, hysterotomy, or hysterectomy will be the best possible procedure. Roentgenography, after the injection of opaque oils or aqueous media and gas, produces clear visualization of the cavity of the uterus and tubes, and pictures vividly the exact conditions existing within the tract. Armed with exact preoperative data the surgeon is able to decide upon the best possible therapeutic measures. The choice of oil or gas as the medium to be employed varies with the purposes and indications of each individual case. In my own experience I have found that injection of iodized oil not only supplements but frequently supplants the insufflation of gas.

Since the list of workers in this field of procedure has been rapidly increasing, I shall omit for the present any discussion of priority, as I have taken up the matter extensively in my monograph: "Gynecological Roentgenology,"[2] where a section has been specifically set aside for the purpose of historic review.

One of the first of the valuable advantages gained by roentgenography has been the accurate estimation of obstructive sterility. Such is the precision that the exact site of blockage is distinctly demonstrable, a result *not* attained by insufflation methods. The place of obstruction determines the site at which the stoma should be made. When the occlusion is in the distal portion of the tube, salpingograms indicate how much of the tube must be resected. The farther the occlusion lies from the uterine cavity the more suitable is the case for plastic operation, and the greater the possibility of subsequent fecundity. Cases with occlusion at the ostium abdominale lend themselves most favorably to operative correction. (See Figs. 3–6.) In order to evaluate the surgical result, opaque oils should be injected repeatedly after operation; this will moreover tend to prevent secondary closure of the stoma.

Salpingography has been conspicuously valuable in obstructive sterility, in many instances making possible the conservation of tubes which otherwise might have been needlessly ablated. Often the preservation of these tubes has an essential influence on the mental outlook of the patient.

In making differential diagnosis of uterine fibroids and ovarian cysts, roentgenography after injection and insufflation definitely classifies the nature of the

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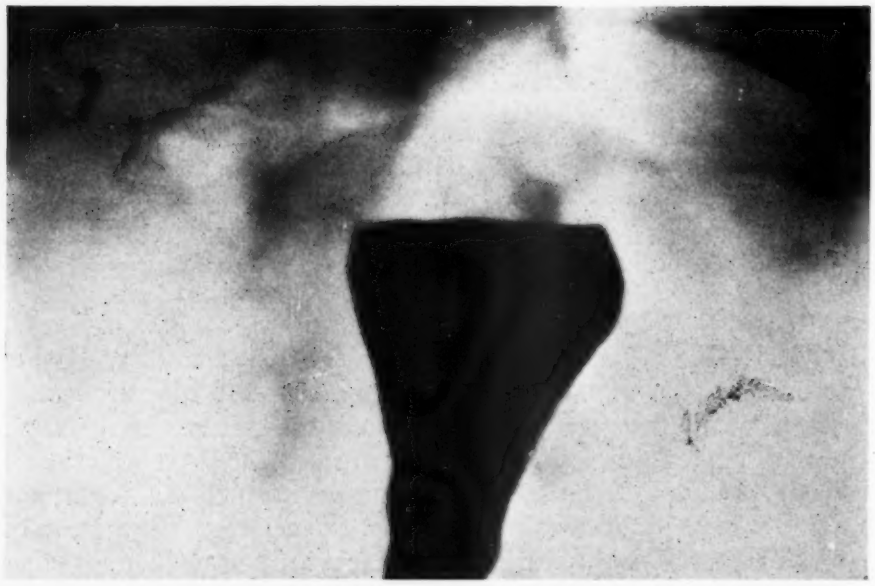

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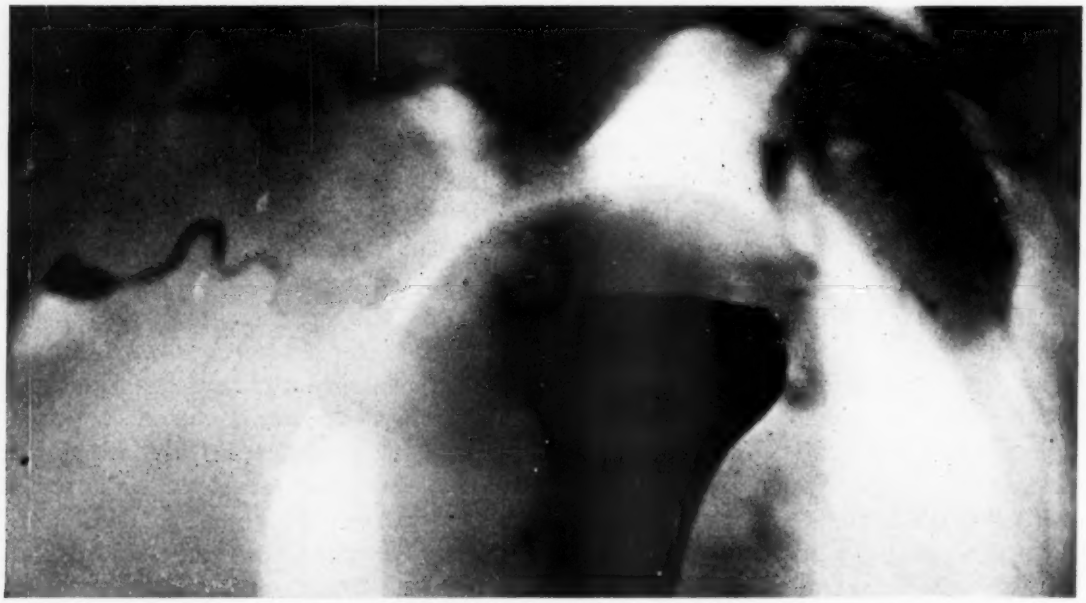

FIGS. 1 and 2. Physiologic contraction of uterine components.

FIG. 1. Patient prone. Transuterine insufflation of carbon dioxide, 1000 c.c., followed by peruterine injection of iodized oil, 4 c.c. External outline of uterus and normal triangular uterine cavity are both clearly seen. Myometrium is relaxed, as shown by rounded contour of cornua. Left tube (reader's right) is not seen; whether this is pathologic or due to physiological contraction cannot be determined from this single film. Entire lumen of right tube (reader's left) is faintly outlined.

FIG. 2. Patient prone. Both enlarged fibrotic ovaries are seen. Lumen of left tube (reader's right) is faintly outlined in distal portion. Proximal ends of both tubes are hardly visualized, apparently because of physiologic contraction.

Observe that physiologic contraction and relaxation of tubes and uterine sections are not always synchronous.

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FIGS. 3–6. Primary sterility. Bilateral chronic salpingitis with ampullary hydrosalpinx.

FIG. 3. Triangular shadow of normal uterine cavity and lumen of both tubes are clearly visualized. Isthmial portions of tubes appear straight and stiff, often an indication of chronic inflammation of tubes. Ampullae are wide and distended. Oil is arranged in droplet formation of "pearl clusters," a further indication of an old inflammatory process, hydrosalpinx of ampullary portion of tubes.

Cannula is seen above triangular uterine shadow impinging on uterine wall. This is due to faulty technique and leads to complications, as endometrium and uterine musculature are likely to be injured and intravasation or injection of uterine blood vessels occurs. Speculum is observed in vagina. It is best to remove speculum during film exposures because by retaining it, thus, some pathologic condition may be concealed by instrument and therefore may not be recorded on film.

FIG. 4. Oil in droplet formation of "pearl cluster." Tubes became patent. Some oil entered peritoneal cavity and is held in adhesions.

neoplasms. Ordinary roentgenological examination in gynecology is practically limited to the diagnosis of dermoid cysts and calcified fibroids, the latter discerned by their mottled appearance of piled up shells or by the resemblance to a calcified sponge. By uterosalpingography, however, it will be observed that in ovarian neoplasms the uterine shadow remains unchanged although at times it is somewhat displaced. In myomas, on the other hand, there is often not only a change in the form and a distortion of the uterine shadow, but also evidence of atony of the walls of the uterus, as revealed by the increased capacity of the uterine cavity. (See Figs. 9

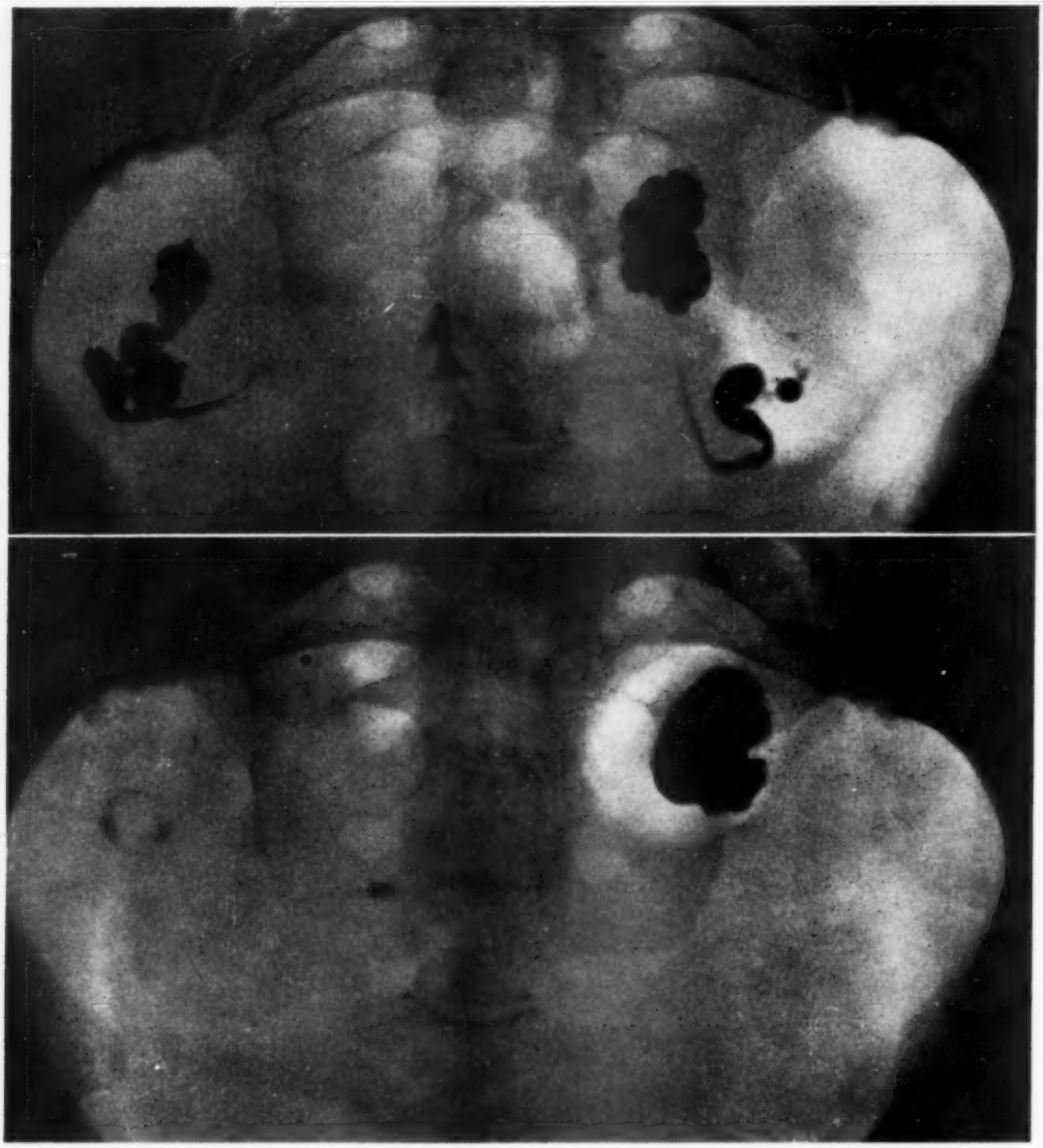

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Fig. 5. After removal of occluding rubber acorn, most of contrast medium emptied itself from uterine cavity. Some of it is still retained in distal portions of tubes. Droplets of oil are observed exuding from tubes in "pearl cluster" formation and are retained in adhesions in abdominal cavity.

Fig. 6. One week later. Oil has disappeared from general peritoneal cavity; a small quantity is still retained in a mass of adhesions on right side. Remaining oil may yet be absorbed, although sometimes it becomes encapsulated, and then represents one of infrequent untoward results.

and 10.) A normal uterus with its tubes will be filled by 3 to 5 c.c. of oil. Senile uteri may accommodate 1 or 2 c.c. and sometimes will accommodate 3 c.c. Uteri with relaxed musculature will stretch and admit from 6 to 10 c.c. Fibroid uteri have long and distorted cavities, permitting the entrance of 10 to 20 c.c. of oil or more.

Intravasation of uterine and pelvic blood vessels may be caused by injection of iodized oil performed at the time of approaching menstruation; it might also be due to pathologic changes in the endometrium. Chiefly, however, it is caused by faulty technique, for example, when the cannula is allowed to penetrate the endometrium forcibly, at times even perforating it and pressing upon the uterine musculature. Intravasation may also result from undue exertion of high pressure during the injection. I have proved this experimentally.[3]

In my opinion this complication may be avoided by proper selection of time and by judicious choice of cases for injection, by gentle technique and control of pressure by a manometric apparatus. Because of the strict adherence to these precautions, I have never encountered any such complications in my own personal cases.

The presence of fibroids is detected by bizarre distortion of the uterine shadow. In submucous fibroid, caution must be observed in order not to inject too large a quantity of opaque medium, as it may surround and submerge the neoplasm and lead to misinterpretation and erroneous diagnosis.

To elucidate minute changes, both physiological and pathological, in uterine mucous membrane, the use of small quantities of opaque medium is advised. The advantage of using small quantities under low pressure is that folds of the endometrium are thus left practically undisturbed. This gives an accurate detailed shadow which is more significant than one artifically smoothed by excess of oil. In ordinary uterograms, fine details of mucous membrane are submerged by the larger volume of media injected.

In the use of smaller quantities of oil for roentgenographic study of details, just enough pressure should be employed to permit easy flow of the medium into the uterus long enough for film exposures. After this larger amounts of oil may be injected and additional uterosalpingograms may be taken.

After a small amount of oil is injected it is necessary to massage the uterus with one finger in the rectum and one hand on the abdominal wall to facilitate the deposition of a thin layer of medium over the entire surface of the endometrium. By applying small amounts of ordinary media to the study of extirpated uteri I have obtained uterograms showing great detail of endometrium. In studies of living uteri I have not been able to demonstrate the finer degree of endometrial detail, apparently because the oily media are insufficiently adhesive. It is hoped that these requisites will be met by new media, especially adapted to the local requirements of the genital tract.

Guthmann and Stähler[1] maintain that they have succeeded in devising a substance which satisfies all prerequisites. It is said to be a good contrast medium which mixes well with uterine and cervical secretions, is thin enough to fill small crevices, and is harmless and well tolerated.

Despite the fact that I have preferred to avoid the use of fluid media in cases of carcinoma, I think that there may be no harm in the cautious introduction of small quantities if excessive pressure be avoided by strict manometric control. In this manner polypose, ulcerative and carcinomatous lesions can be definitely located; this is advantageous especially in cases requiring direct attack with radium or curette.

Since uterosalpingography outlines and maps out the normal and abnormal states of the pelvic viscera, the uterus and its tubes, malformations and displacements are plainly visualized. Sharp anteflexion or

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FIGS. 7 and 8. Primary sterility. Independent action of uterine components.
For captions see opposite page.

retroflexion is denoted by the foreshortening of the vertical diameter and the base of the shadow of the uterine cavity observed to be on a lower level than the isthmus of the uterus which is directed upward.

As it often happens that physiologic

Figs. 9 and 10. Uterosalpingogram: Soft myoma of uterus. Distorted uterine cavity. Relaxed state of uterine musculature.

S. G., aged forty-four years, three children, youngest child seventeen years old. Had menorrhagia for five years, and for last two years menorrhagia and profuse metrorrhagia. Patient complained of discomfort in lower abdomen. Pelvic examination revealed a large, smooth, elastic mass filling out pelvis, continuous with cervix, and extending upward about 5 cm. above pubis. Cervix was eroded and lacerated. A large polyp protruded from cervical canal. Introitus was relaxed. Diagnosis was soft myoma of uterus, polyp of cervix and rectocele.

After combined transuterine insufflation of 600 c.c. carbon dioxide and peruterine injections of 3, 5, and 8 c.c. iodized oil, a series of film exposures was made. An insufficient amount of carbon dioxide having been introduced, external outline of neoplasm was not distinct. Therefore air was insufflated into urinary bladder with hope of bringing out external outline of mass more distinctly.

Fig. 9. After insufflation of carbon dioxide, injection of 8 c.c. iodized oil, and air insufflation of bladder, this film shows large mass reaching up to second sacral segment with lower limit outlined by carbon dioxide and air in bladder. Entire fundus of uterine cavity is filled out and displaced to right. Right cornu is rounded due to relaxation of musculature. Lumen of left fallopian tube is shown for 0.5 cm. at its proximal end. Its ampullary end is also seen, with oil exuding through ostium abdominale into free peritoneal cavity. Rest of tube is not shown on account of physiologic contraction. Uterine cavity is elongated and distorted by myoma.

Fig. 7. Note triangular shadow of normal uterine cavity, contraction of uterus at internal os, cornual sphincters distinctly outlined. Right tube (reader's right) is occluded in middle of isthmial portion. Left tube is occluded at beginning of ampulla. Injection of iodized oil had tendency to dilate proximal portions of tubes. In such cases oil aids drainage of tubal contents into uterus, thus producing a therapeutic effect on inflammatory process.

Fig. 8. After removal of occluding acorn, body of uterus is not shown as it has contracted and expelled its contents into vagina. Cornua and patent proximal portions of both tubes are distinctly visualized. In this case two components of uterus, both cornua, did not participate in contraction of third component, body of uterus. (Cf. Figs. 21–23.) Vagina is distinctly outlined. Note stretched-out right fornix of vagina, a consequence of an old inflammatory process in pelvis. This is further evidence of same condition which produced occlusion of tubes.

contraction and relaxation of the uterus and tubes occurs during the exposure of the films, it is advisable to take several films so that a misleading diagnosis of filling defect of the uterus or of blockage of a tube will not result. Uterine and tubal contractions and relaxations are in reality physiologic responses due either to the stimulating effect of the foreign substances introduced, or to the altered intrauterine pressure. These physiologic responses of uterine contraction and relaxation may be enhanced by the hypodermic injection of pituitrin.

In the study of uterosalpingograms, a snare-like contraction can be observed at the junction of the tube and cornu. (See Figs. 7–8, 24–25, and 35.) This has been interpreted by some observers as due to the presence of a sphincter, called a tubal sphincter. Others consider it not a tubal, but a uterine structure. After an intensive study of the subject, I am convinced that a sphincter is present and that it is a uterine structure. I believe it should be called "cornual sphincter."

Fig. 10. Roentgenogram of extirpated uterus. After hysterectomy cavity was refilled with iodized oil and exposures made. Note same general outline of uterine cavity as in Figure 9, except that right cornu is in tonic contraction as indicated by its pointed appearance and by sharp outlines of margins of uterine shadow. Part of right fallopian tube now visible; evidently in preceding film it was physiologically contracted.

That it is a uterine structure can be confirmed by a study of microscopic sections of the uterotubal area which exhibits a distinct circular arrangement of most of the muscle fibers of this section, and is lined with uterine mucous membrane. The existence of a sphincter can be proved by its constant presence at one and the same

point, no matter what the physiologic changes may be in this area.

However, we cannot refute entirely the assertion of those who argue that this contraction is due not to a sphincteric action but state that it is simply a functional condition. Their claim may be supported by the fact that in many instances I have found in uterosalpingograms of both living and extirpated uteri that not only the annular contraction is visible, but the rest of the uterus is likewise in a state of tonic contraction, as indicated by the sharply pointed cornua, sharply outlined margins of the uterine cavity, and the contraction of the uterus at the isthmus. (See Figs. 25 and 35.) On the other hand, we occasionally find uterograms of both living and extirpated uteri in the relaxed state which despite the uterine relaxation show persistence of a distinct annular contraction at the uterotubal area. (See Fig. 24.) This then would speak strongly for the argument that the annular contraction of the uterotubal area is due to an anatomic sphincter.

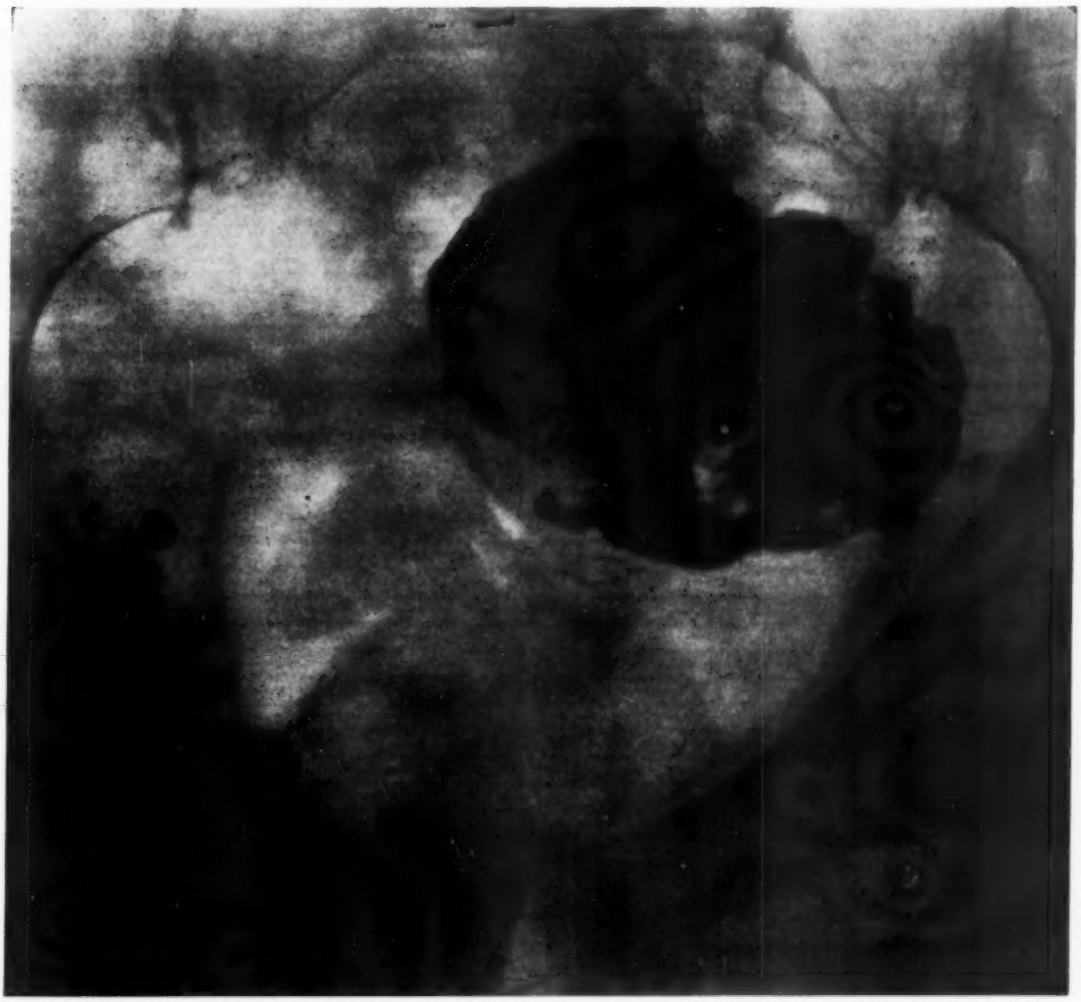

Fig. 11. Calcified fibroid. Note irregular, mottled appearance of fibroid resembling a calcified sponge to be differentiated from calculi of urinary bladder with smooth, concentric, lamellated shadow rings of equal density. (See Figs. 12 and 13.) (Courtesy of Dr. Travers.)

We also know that the uterus does not contract en masse, but sectionally and alternately. Thus one cornu is contracting while the other is relaxing. (See Figs. 21–23 and 26–29.) This is exactly true of the annular contraction at the uterotubal area.

In roentgenograms, this section appears alternately in the contracted and in the relaxed state. There must be some mechanism accountable for producing this functional contraction both in the sphincter and the rest of the uterine musculature. However, this is still a moot point, which perhaps will some day be determined embryologically.

In seeking convincing evidence of the anatomic structure of the uterotubal sphincter through a study of the microscopic serial sections, one may easily become discouraged by the amount of patience and labor

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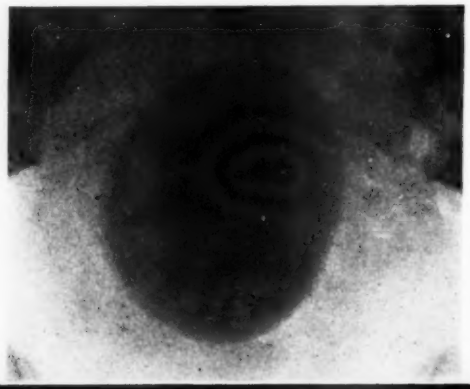

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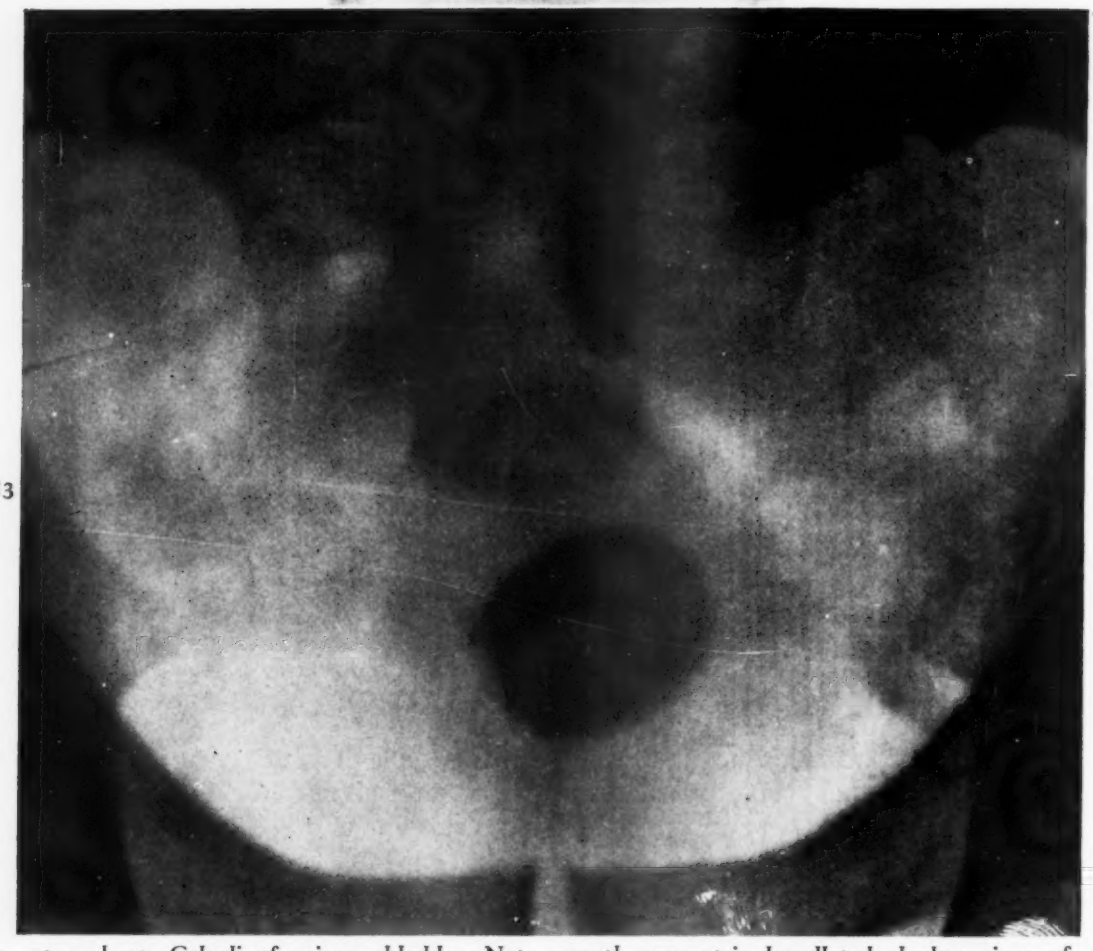

Figs. 12 and 13. Calculi of urinary bladder. Note smooth concentric lamellated shadow rings of equal density, as differentiated from irregular, mottled appearance of calcified fibroids. (See Fig. 11.) (Courtesy of Dr. Travers.)

necessary to obtain the proof. Roentgenographically one is able to locate the sphincter with ease and accuracy, but in first definitely uterine section. The sphincter, microscopically revealed, possesses definite circular and longitudinal muscle

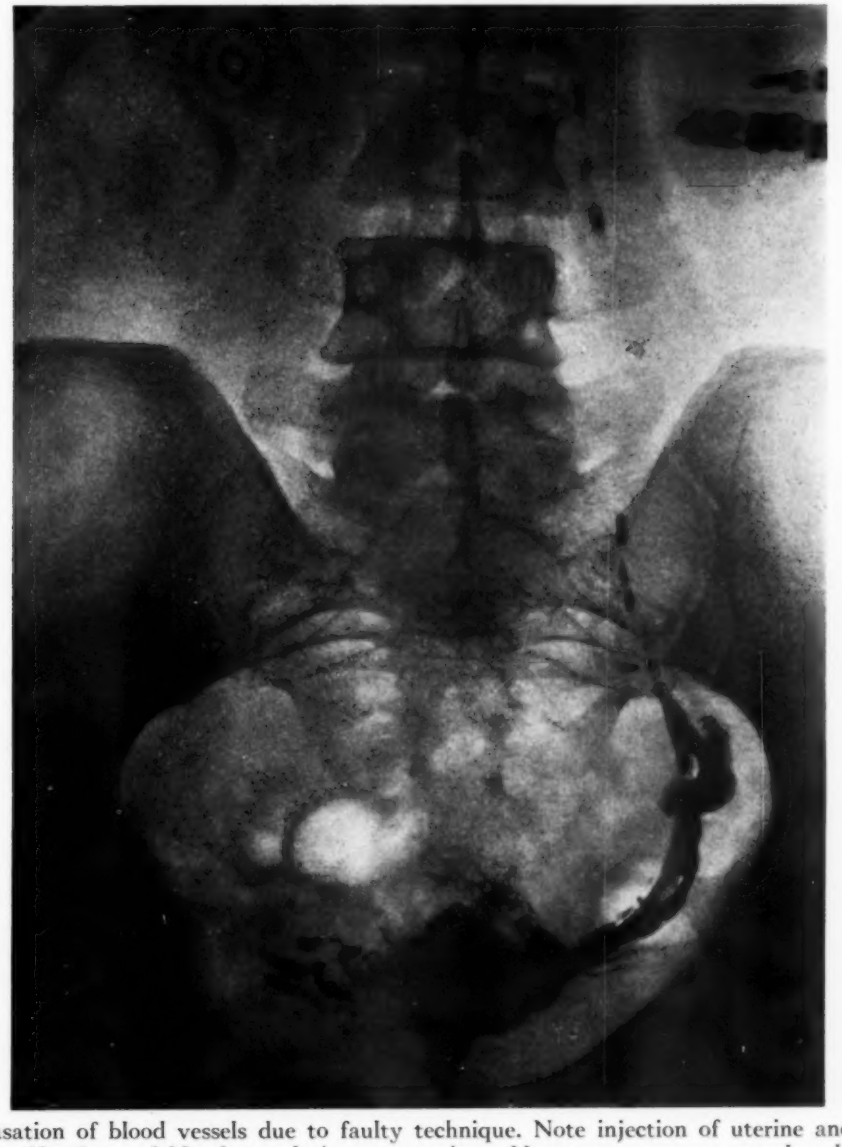

Fig. 14. Intravasation of blood vessels due to faulty technique. Note injection of uterine and ovarian blood vessels and ramifications of blood vessels in myometrium. No manometer was employed. Evidently too much force was used by physician who introduced iodized oil.

making the sections of the substratum of the sphincteric area, one may miss by a few micra the very section embodying the annular arrangement of muscle fibers, which compose the anatomic apparatus of the sphincter. Definite tubal sections and definite uterine sections present no difficulty and it is entirely possible to determine the last definitely tubal section and the bundles, and anatomically corresponds to that part of the uterine apparatus which in the roentgenogram following the injection of opaque media shows a distinct snare-like contraction. (See Fig. 35.) It must be realized however that hundreds of sections must be made and the point of transition of the uterine cavity into the tubal lumen histologically established before one is

FIG. 15.

FIG. 16.

FIGS. 15 and 16. Effect of intrauterine injection of iodized oil after curettage.

Fig. 15. Extirpated uterus was injected with 4 c.c. iodized oil under low manometric pressure. Note triangular outline of uterine cavity. (After Jarcho, *Med. J. & Rec.*[3]) (See Fig. 16.)

FIG. 16. Extirpated uterus was injured by curettage and a large quantity of oil was reinjected under high pressure into uterine cavity. Note distribution of oil in blood vessels and spaces between bundles of myometrium. Same will occur if rough and injudicious technique is employed in injecting living uterus. This can be avoided by gentle technique, use of some form of manometer, and controlling amount of opaque medium and pressure. (After Jarcho, *Med. J. & Rec.*[3])

FIG. 17. Submucous fibroma. Large fibroid uterus with negative filling defect produced by submucous fibroma and an indentation on reader's right caused by interstitial fibromata. Cornual sphincters are faintly indicated. Both tubes are well outlined. Oil is entering free peritoneal cavity, some of it is in droplet formation indicating inflammatory process of tubes.

Submucous fibroma was larger than its shadow on film indicated, but it was partially submerged by large amount of oil injected. Smaller quantity would have brought out entire shadow of submucous fibroma far more distinctly.

FIG. 18.

FIG. 19.

FIGS. 18 and 19. Submucous fibromata.

FIG. 18. Roentgenogram of extirpated fibroid uterus with submucous fibromata. Fibroid of this size, ordinarily, could have been treated with *x*-ray or radium, but submucous fibroma was a contra-indication and therefore hysterectomy was done. (See Fig. 19.)

FIG. 19. Extirpated uterus with multiple fibroids, same as Figure 18. Uterine cavity is split open to show submucous fibromyoma. Diagnosis of such cases can be made by uterosalpingography. If treated by roentgen rays, these patients are likely to bleed profusely after treatment. If radium is inserted, necrosis of submucous fibroma may take place.

FIG. 20. Extirpated fibroid uterus injected with small quantity of oil under low pressure. Shadow of uterine cavity appears irregularly mottled and serrate, due to presence of numerous polypoid protrusions. Latter would have been concealed by use of larger quantities of oil. External contour of uterus bespeaks presence of fibroids.

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FIGS. 21–23. Independent action of uterine components.

FIG. 21. Sharply anteflexed uterus denoted by foreshortening of vertical diameter and base of triangular shadow of uterine cavity on a lower level than isthmus of uterus. Fundus is practically resting on upper margin of pubis. Both tubes are occluded at uterotubal junction. Cervical glands are injected and cervical canal is dilated. Left cornu (reader's left) does not show on account of its complete contraction. Right cornu is rounded and indicates relaxation. Uterine shadow gives appearance of a "drooping lily."

Note only one cornu is contracted, illustrating that all three components of uterus do not always act synchronously.

FIG. 22. Sharply anteflexed uterus, foreshortening of vertical diameter, occlusion of both fallopian tubes at uterotubal junction. Good uterine tonus is indicated by pointed cornua and sharp outlines of uterine shadow. Left cornu (reader's left) has reappeared. Right cornu is beginning to contract as shown by its pointed appearance. Cervical glands are well filled and cervical canal is dilated.

prepared to confirm or deny the existence of the anatomic cornual spincter. (See Figs. 33 and 34.)

Fig. 23. Patient prone. Sharply anteflexed uterus with fundus (base of triangular shadow) on lower level than isthmus. There is marked contraction of entire uterine cavity and oil fills out only fundus. Body of uterus and isthmus are scarcely visualized on account of general contraction of lower uterine segments. Cornua are pointed. Part of left tube (reader's right), curled on itself, is faintly outlined, indicating chronic inflammation. Right tube (reader's left) is not visible, but there is marked contraction of cornual sphincter and drop of oil appears distally from it. Cervical glands are injected and cervical canal is slightly filled.

Note again uterine components sometimes contract and relax independently of each other. (Cf. Figs. 7–8, 26–29 and 30–32.)

Although it may be properly assumed that untoward results may follow the possible introduction of septic material from the tubes into the peritoneal cavity after the injection of iodized oil or insufflation of gas, I have never encountered any such cases in my own experience. In the main this may be attributed to a very careful selection of cases. When we consider however that insufflation of gas and the introduction of opaque substances into the uterus and tubes has been the practice of countless workers of varied skill and experience, the reports of unfavorable or damaging results have been comparatively few.

In my belief, contraindications to uterosalpingography include cardiac disease, gonorrhea, and acute tubal inflammation; malignant growths of the uterus, because of the danger of carrying the cancer cells into the peritoneal cavity; menstruation and profuse bleeding and pregnancy, unless therapeutic abortion is contemplated.

I may add here that some very able French workers have treated acute and subacute conditions with iodized oil (a practice I do not recommend however) and they maintain that beneficial effects have resulted, the iodized oil preventing closure of the tubes.

I avoid injection of iodized oil during menstruation for fear of having endometrial tissue carried into the peritoneal cavity and producing endometriosis and of possibly penetrating the endometrium and forcing the oil through the wounded mucous membrane into the muscular wall or blood vessels. In uterosalpingograms, endometriosis (adenomyosis) of the uterine wall is indicated by irregular protrusions or diverticula extending out from the triangular shadow of the uterine cavity.

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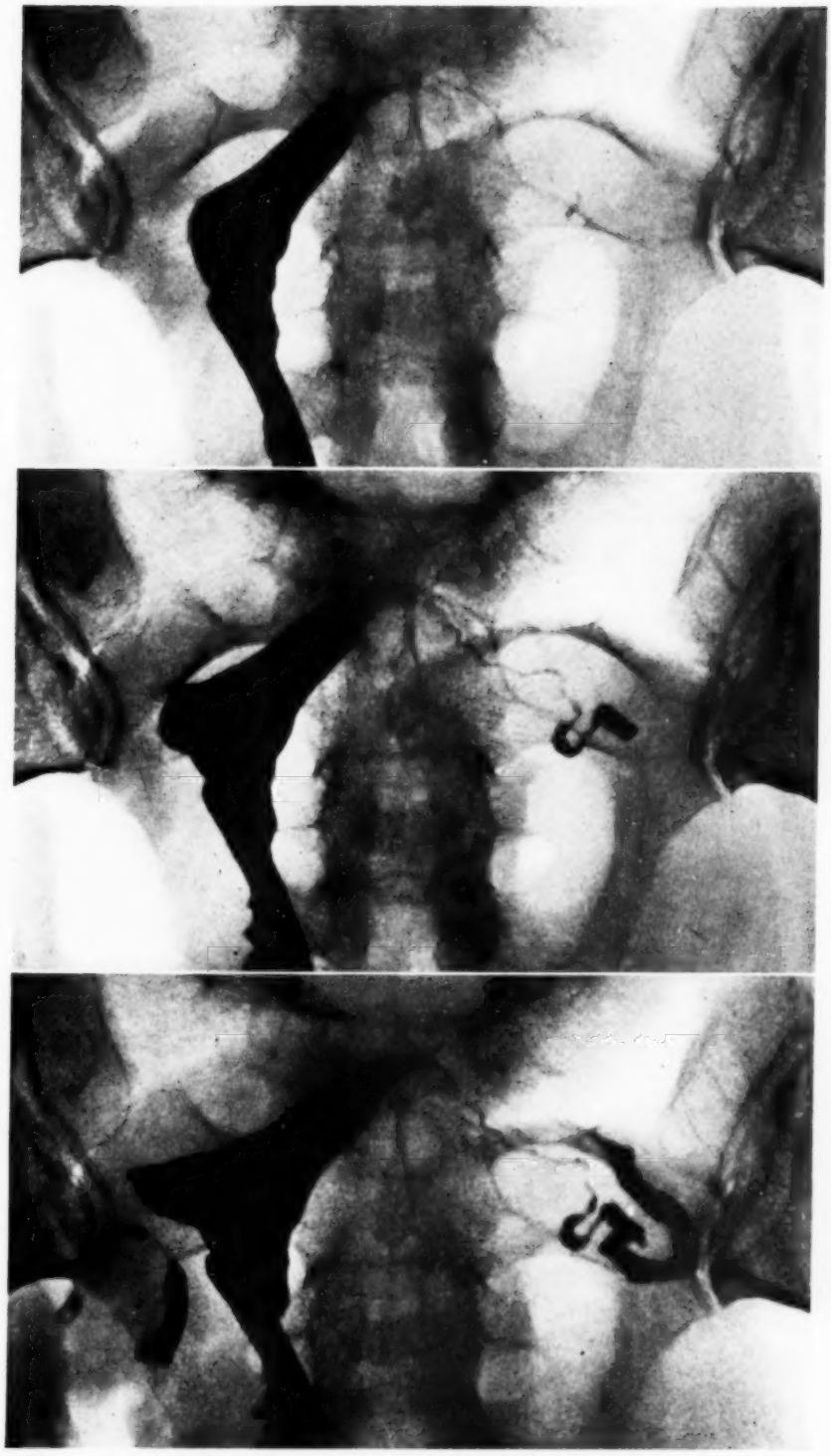
FIGS. 24 and 25. Primary sterility. Occluded tubes becoming patent.

FIG. 24. Right cornu (reader's right) and margins of uterine shadow are rounded indicating relaxation of uterine musculature. Left cornu (reader's left) and snare-like contraction (or cornual sphincter) are clearly visible. Oil is seen in beginning of proximal portion of left tube. It cannot be determined from this film alone whether tubes are occluded or in a state of physiologic contraction.

FIG. 25. Cornual sphincters. Entire uterine cavity is filled and in a state of tonic contraction as indicated by pointed cornua, and sharply outlined margins of uterine shadow. Both cornual sphincters are contracted as shown by snare-like compressions at cornua. Both tubes are filled throughout their extent. A drop of oil is evident at fimbriated end of right tube (reader's right). Left tube is curled on itself behind uterus although ampulla is distinctly visualized. It cannot be determined from this alone whether or not tubes are patent at ostia abdominalia. Some oil is observed in cervical canal.



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FIGS. 26–29. Independent action of individual components of uterus.
For captions see page 30.

In some cases of chronic salpingitis and occlusion of tubes at points in the distal portion, the injection of iodized oil has the tendency to dilate the proximal portions of the tubes and encourage the drainage of the tubal contents into the uterus. This may exert a favorable influence upon the pathologic changes in the tubes, as will be shown in several illustrations. (See Figs. 3–6 and 7–8.) I have observed chronically inflamed tubes become functionally useful after iodized oil injections.

Curettage or abrasions of the uterine mucous membrane should be most assiduously avoided for fear of causing air embolism when gas is employed or possibly the injection of the blood vessels of the uterine musculature with oil or even the intravasation of the pelvic blood vessels during the iodized oil injection. (See Figs. 14, 15 and 16.)

Abortion cannot be induced by the injection of iodized oil unless the ovum is injured by the cannula or the amount of

Fig. 29. Twenty-four hours later. Shows dissemination of oil in peritoneal cavity.

Fig. 26. Right cornu (reader's right) is well filled. Cornual sphincter is shown. Small quantity of oil is entering right tube. Left cornu and left tube are *not* visualized. Whether filling defect is due to pathologic cause or to physiologic contraction cannot be determined from this film alone.

Fig. 27. Right cornu and right cornual sphincter are clearly visualized. Lumen of right tube is filled throughout its extent. Small quantity of oil is exuding from ostium abdominale into peritoneal cavity. Left cornu is beginning to appear, but left tube is still not visible.

Fig. 28. Triangular shadow of normal uterine cavity is seen in its entirety. Right cornual sphincter is present. Lumen of right tube is shown in its entire extent. Large amount of oil is entering peritoneal cavity through ostium abdominale of right tube. Left cornu is distinct. Left cornual sphincter is beginning to appear. Proximal portion of isthmus of left tube is not visualized. Since distal portion of tube is filled, proximal portion must be patent but is evidently physiologically contracted during exposure of this film. Oil is beginning to enter peritoneal cavity through fimbriated end of left tube.

Observe in Figures 7 and 8 that various tubal and uterine components do not contract and relax synchronously.

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FIGS. 30–32. Synchronous contraction of three uterine components.

Fig. 30. Patient prone. Triangular shadow of normal uterine cavity, pointed cornua indicating good uterine tonus, contraction at isthmus of uterine cavity, spindle-shaped cervical canal, and cervical glands well filled. Right tube (reader's left) is filled up to beginning of ampulla. There is a slight physiologic contraction at proximal portion of right tube. Left tube is outlined throughout its extent and shows beginning physiologic contraction about 0.5 cm. distally from cornu.

FIG. 31. Patient prone. Occluding acorn has been removed. Note triangular uterine cavity is smaller than it appeared on preceding film (Fig. 30). This is due to uterus emptying itself by a general collapse like that of a deflating balloon, one of several methods of uterine evacuation. External outline of body of uterus is also visible. Both tubes are filled throughout their extent. Oil is escaping through ostia abdominalia. Right cornu (reader's left) and proximal one-third of right tube are contracted at proximal end, although it is filled throughout its remaining extent. Cervical canal is emptying itself but some oil still remains in cervical glands. Very faint outline of vagina is shown.

This illustration shows oil emptying from uterus by synchronous contraction of three uterine components, that is, both cornua and body of uterus, expressing oil into peritoneal cavity through both tubes and through cervical canal into vagina. (Cf. Figs. 7–8, 21–23 and 26–29.)

oil is so massive that the volume causes damage to the ovum. This has been verified by many experimenters and by myself. I had hoped that therapeutic abortion would be effected after injection in a patient three months pregnant, whose systolic blood pressure was 250. I was finally compelled however to empty the uterus surgically as the injection failed to produce the desired result.

Fig. 32. Five minutes later. Patient prone. After more oil has escaped, uterine cavity still maintains its outline although it has decreased appreciably in size as compared with that in two preceding films (Figs. 30 and 31). Oil is being discharged through both tubes into peritoneal cavity and through cervical canal into vagina. Proximal ends of both tubes are not visualized on account of their physiologic contraction. Cervical canal is faintly outlined. Cervical glands are filled. Triangular shape of vagina is more distinctly outlined.

Mendenhall[4] reports 3 cases where the intrauterine injection of iodized oil aided in the recognition of an extrauterine pregnancy, a difficult differential diagnosis to make even when a flat roentgenogram discloses the skeleton of the fetus. The uterosalpingogram was that of a nonpregnant uterus, thus definitely locating the pregnancy in the free abdominal cavity. Nölle[5] has described a similar case where this differentiation was impossible until he had resorted to an iodized oil injection leaving it to the subsequent roentgenograms to define the exact location of the pregnancy.

Although it cannot be claimed that the use of opaque media and roentgen examination leads to infallible diagnosis, it can certainly be maintained that diagnostic precision is greatly increased thereby. Sigwart[6] reports an interesting instance of a patient operated upon for right diseased adnexa. The ampulla of the right tube was removed. After operation an abdominal fistula developed through which a cyclic discharge or menstrual blood exuded from the sinus. Peruterine injection of iodized oil followed by a uterogram showed a connection between the abdominal fistula and the remaining portion of

the tube. Laparotomy confirmed this diagnosis.

The technique is simple, but strict aseptic precautions must be taken. Gentleness of manipulation will gain the patient's cooperation and confidence, will facilitate the work, and will lead to good results with few or no complications. The interpretation of the films requires experience which is easily acquired by a study of the plates, clinical findings, reference to previous films, cases and reports of postoperative findings.

It is almost needless for me to mention that the earnest cooperation of the gynecologist and roentgenologist is essential for good results.

Fig. 33. Microphotograph: last tubal section showing beginning formation of cornual sphincter. Mucosa still shows characteristic folds of tube. Epithelium of tube is of simple columnar ciliated type.

CONCLUSIONS

Uterosalpingography, or the roentgenological visualization of the uterus and fallopian tubes after peruterine injection of opaque oils, and the perabdominal or transuterine insufflation of gas is an accepted, harmless, and valuable means of exact gynecological diagnosis in selected cases.

Uterosalpingography is of the utmost value:

1. In establishing the patency or nonpatency of fallopian tubes and definitely locating the site of blockage in cases of occlusion.

2. In restoring the patency of occluded tubes.

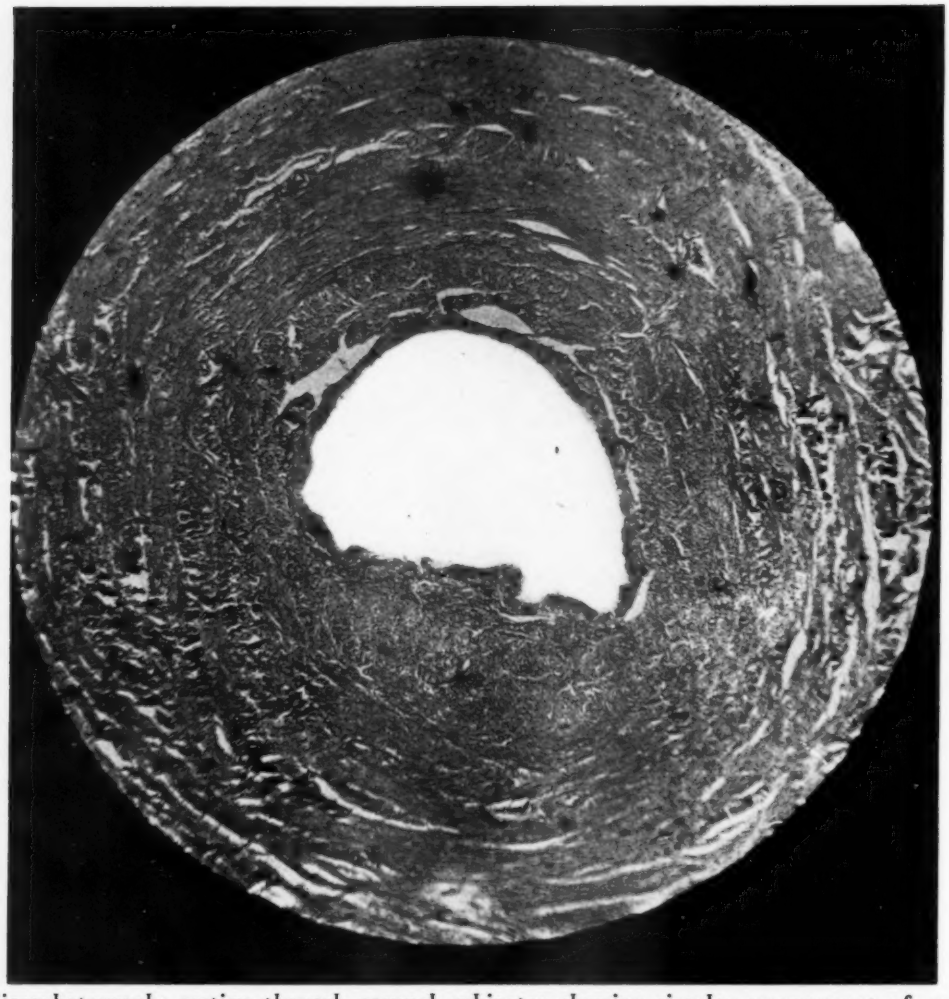

FIG. 34. Microphotograph: section through cornual sphincter showing circular arrangement of muscle fibers. Mucosa assuming characteristics of uterine mucosa. Epithelium is of simple high columnar ciliated type.

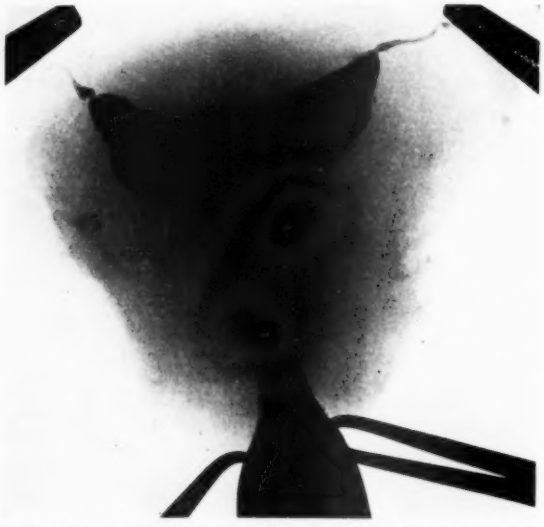

FIG. 35. Cornual sphincter. Persistent muscular tonus in extirpated uterus of patient with papillary adenocarcinoma of ovaries, as observed after injection of 5 c.c. of iodized oil, one-half hour after extirpation. Both cornual sphincters are clearly visualized; left sphincter more contracted than right. Uterine contraction is indicated by pointed cornua and sharp outline of margins of uterine shadow.

3. In suggesting the best site for a stoma in operations on sealed tubes or in indicating the part of the tube to be resected.

4. In determining the success of salpingostomy and preventing the stoma from contracting and closing secondarily.

5. In the diagnosis, prognosis, and treatment of chronically inflamed and occluded tubes.

6. In deciding, in cases of fibroids of the uterus, upon the most advisable therapeutic procedure, whether surgical interference, roentgen, or radium treatment.

7. In making a differential diagnosis, in settling differences of opinion in pelvic diagnosis, and in providing a permanent record for future reference.

8. Special mention is made of the use of small quantities of media for studies of finer endometrial detail.

9. The cornual sphincter is discussed.

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UTERINE CANCER AND ITS TREATMENT BY RADIUM*

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THE day has arrived when I believe we should proclaim that cancer is surely curable. It is in the incipient stage of cancer that proper treatment produces the greatest number of cures. Incurable cancers are almost invariably the result of failure of early recognition of the disease. Wise propaganda will disseminate to the public facts about cancer which should be within the knowledge of every man and woman. It will impress upon the public and the practitioners of medicine, the family doctors, the importance of early and periodic advice based upon accurate diagnosis. Nothing will lend greater encouragement to the public at large than assurance that cancer *is curable.*

In the campaign against cancer, all possible resources must be utilized. Until the exact cause has been determined and a specific cure has been found, our aims in this fight must be:

(1) To remove, in the individual patient, the unhealthy conditions which we have learned precede cancer, and thus prevent it.

(2) To make an early diagnosis while the disease is still manifestly local, and to educate the public to realize that early diagnosis is necessary.

(3) To treat the disease immediately, radically and thoroughly.

To recount the probable etiological factors of cancer would necessitate a boresome recital of timeworn facts well known to each and every one of us. It would be decidedly too academic. We all recognize the fact that chronic irritation plays an important part in the causation of malignancy. We know that the simple pathological disturbances of the cervix are oftentimes a fertile field for the implantation of the disease. It is evident, too, that by the early removal of this disease condition through destruction of erosions, repair of lacerations and the relieving of inflammatory processes, malignancy may be prevented. The actual exciting cause of cancer is, of course, still unknown. I have the temerity to state that I believe that, eventually, it will be explained through the medium, or upon the basis, of endocrinological dysfunction. While it is theory, at best, one cannot pass over the fact that cancer usually makes itself known at a period following an extreme and obvious endocrine upset. The appearance of cancer coincidently with the picture of glandular disturbance at the climacteric and about the menopause is too patent. We know that malignancy manifests itself more quickly and is more fulminating in its growth at that time when endocrine imbalance is noticeable. It is slower in growth where there is a cessation or diminution of function of the ductless glands as is seen in old age. When a woman is seemingly most healthy, yet in the midst of her climacteric, we usually see the most cancer. It seems not a too far-fetched idea that there must be some lack of inhibition or some abnormal stimulation of cell growth due to the lack of correlation of glandular activity which alone allows for the mitosis characterizing malignancy.

The subject of early diagnosis has received much consideration, but the last word will not be said for many years to come. Extensive propaganda by physicians has undoubtedly brought many women for examination who would otherwise have received no attention until their malignant conditions were well advanced. In order to begin treatment when the lesion is still

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incipient, it must be brought to the physician before the well-recognized symptoms of intermenstrual or post-menopausal bleeding and discharge are in evidence. The only way that this can be accomplished will be by careful observation of all gynecologic patients who are within the "cancer age" limits. No pelvic examination should be considered complete unless the examiner has satisfied himself that nothing of a malignant nature is present in the uterus or adnexa. Unless he takes pains to search for them, the earliest manifestations are practically certain to be overlooked.

One should not rely wholly upon the macroscopic picture in making a decision for or against cancer of the cervix. The small, cerise, velvety erosion may be easy to diagnose, but if it bleeds when touched by the examining finger or through sexual or instrumental trauma, it takes on a cancerous aspect. I rely entirely upon biopsy and examination of the tissue in any suspicious erosion, and I believe we have no right to neglect this procedure. Through maldiagnosis we tinker with too many cervices and resort too often to ineffective cauterization and coagulation, this treatment and procrastination allowing for spreading of the malignant condition. In any case of suspicious cancer of the fundus, a diagnostic curettage should be done, followed immediately by a frozen section diagnosis. I insert my intrauterine radium at the time of operation and am guided as to my dosage according to the report of the pathologist.

A knowledge of the so-called precancerous changes in the endometrium is imperative in all who undertake gynecological examination. Ewing says, "A simple overgrowth of surface epithelium with partial or complete epidermization cannot be regarded as a definite approach toward a neoplastic process. Yet the distinction between such benign overgrowth and progressive malignant process is extremely difficult, and opinions differ as to the essential morphology of this early form of corpus carcinoma."

The importance of syphilitic lesions of the cervix as a possible predisposing factor in the cause of malignant change is now well recognized, and a recent paper by Martzloff of Portland, Oregon, calling attention to leucoplakia of the cervix uteri as a probable manifestation of cancer in its earliest form, is decidedly interesting. The work of Hinselmann shows that histological examination of these cervical areas generally revealed a picture compatible with leucoplakia, in which the finer histologic details varied from more epithelial hyperplasia to those changes ordinarily associated only with the cytology of malignancy but without invasion.

My attention was recently called by Dr. Joseph Muir to the importance of leucoplakia of the uterus in the etiology of cervical carcinoma, and the possibility of early recognition of this lesion as being definitely malignant in character. Leucoplakia is commonly supposed to be luetic in origin and is, therefore, regularly classed as benign. The benignity of any of the tertiary epithelial manifestations of syphilis is rapidly coming more and more into question. Leucoplakia is a form of epidermization of the endometrium now and then seen with curettage, or the removal of uterine polyps, more often found in the corpus than in the cervix. Some pathologists have attributed its presence to survival of fetal endometrium, but Dr. Muir thinks it not unlikely due to a spirochetic infection conveyed through intercourse. Most women showing it will give a 4-plus Wassermann reaction.

Before the discovery of radium by Madame Curie, the treatment of cancer of the cervix uteri was by local destruction of the carcinomatous tissue with some form of cauterization or by surgical operation. I can well remember the cautery at the Maine General Hospital in Portland twenty-two years ago, and the way we wielded it. I well remember the ineffectual surgery of the cervix more than two decades ago. Conscientious as were those men of that date, I cannot but shudder

when I realize the terrible mortality coincident with such treatment, and it is interesting to note the great strides that have been made in surgical treatment since that time, and the recent transition from surgery to irradiation of the cervical cancer.

Cancer of the cervix is very unfavorable for surgical operation. The exceedingly high death rate in the operation itself and the small likelihood of benefiting the patient, even if she survives the immediate effects of the operation, make it quite apparent that in this anatomical location, surgery is seldom, if ever, justified.

Favorable results after operation are often misleading: odor is removed, bleeding stopped, the strength of the patient is temporarily better, which tends to offer encouragement to both patient and physician, but the fact that deep implantation has occurred, the cancer cells being transplanted deep beyond hope of possible cure, does not impress itself upon the minds of either patient or doctor. Temporary favorable results are usually only enjoyed by the women who, escaping death at the time of operation, have the good fortune to heal after it. Cases of early cancer of the cervix which are of a type that are easily and surely cured by radium are often made incurable and hopeless by surgery.

Abroad, particularly in Vienna at Simon's Clinic and in France at Regaud's Clinic, early cases, that is those usually designated in this country as "operable," are selected by preference for radium therapy. The idea of using it as a last resort, which still largely prevails with us, has given place to the regular consideration of radium treatment in lieu of surgical excision. The percentage of five-year cures at these institutions is extremely high; their statistics are among the best in the world.

A glance over the literature on the treatment of cervical carcinoma during the past twenty years shows how steadily the tide of favor toward radium has crept up upon the surgical advocates. Each year more and more cases are reported in which no surgical intervention of any kind has been used. After a while we commenced to get five-year reports, then ten-year, and now we are beginning to learn of women who have remained well and cancer free for fifteen years after radium treatment.

Those who resort to surgery of the cervical cancer usually attempt the so-called Wertheim operation as the only efficient intervention. Wertheim and Schauta with their radical hysterectomies gave such improved results over the early operative procedures that for fifteen years or more no other treatment was instituted. The operators who are complete masters of this difficult technique are relatively few. To reach them a woman has often to travel a long distance, and undergo considerable expense. With us, economic considerations frequently prevent women from undergoing operation, or put them into the hands of men inadequately equipped by training or experience to do a complete Wertheim operation. These operations do not figure in the statistics which are adduced to show the good results of "early" surgical treatment. They are lost in the general operative results of small hospitals and private clinics. From the great gynecological centers, and the huge surgical clinics having special gynecological divisions manned by experts, the reports are correspondingly better.

Aside from the dangers and expense of even the operation done in the earliest stages, there is the long disability coincident with any major pelvic operation. The mother of a family shrinks from the thoughts of many weeks of invalidism, even when the economic factor is not a vital one. Protracted convalescence is more dreaded than the actual ordeal of operation.

Compare with this the whole procedure of radium treatment. The primary mortality of the Wertheim operation is charitably estimated at 17 per cent. Radium treatment as at present carried out has no

primary mortality whatsoever. Operative surgery entails a long stay in the hospital, expenses for anesthesia and extra attendance, to say nothing of the "pain and anguish" attendant upon it. I personally believe that cancer of the cervix should be considered a radiotherapeutic entity, and radium alone suffices.

Adenocarcinoma or corporeal cancer and its treatment by radium presents an interesting opportunity for discussion. Where nowadays we treat cancer of the cervix by radium, or radium and deep *x*-rays, in contradistinction to surgery, carcinoma of the body of the uterus allows for a much different proposition. Cancer of the uterine body occurs much less frequently than carcinoma of the cervix (about 10 per cent of the cases) and it has not the same high mortality. The diagnosis is less certain on account of the many other conditions which may simulate it, and because it is not visible to the eye. A difference of opinion exists today among surgeons and surgeon-gynocologists as to whether adenocarcinoma should be considered a radium disease wholly, or a surgical disease. Some take the stand that radium alone should be used and no surgery elected; others believe in hysterectomy and later irradiation if need be, while many believe in preoperative irradiation with subsequent hysterectomy. At the Peham Klinik in Vienna Dr. Simon was rather emphatic that surgery was contraindicated, radium was all-sufficient, and from my small experience, I believe that radium is the treatment to be instituted first, and one may elect hysterectomy later.

In correspondence with Dr. George W. Ward, he tells me that he always radiates the cancer of the fundus and a few weeks later, he performs a pan-hysterectomy, not a Wertheim or a Schauta procedure. He adheres to this technique because he believes that one can never be sure that he has radiated all parts of the cornua and fundus, and there is little mortality with the ordinary hysterectomy in good risk cases. However, 50 per cent of his patients with cancer of the fundus receive only radiation because the others are bad operative risks due to senility, obesity, arteriosclerosis, cardiac and renal disease. In other words he follows his radiation with hysterectomy where practicable.

I believe this is good sense because through radium the condition of the patient is improved and the chance of metastasis through surgical trauma is rendered negligible. Where surgery is first employed, later radium therapy is rendered difficult of application. Operation discloses the true extent of the disease, whereas radium, of course, is handicapped, because the application must be made in an invisible field.

The varieties of technique which have been used since radium therapy was instituted, and a discussion of each, is decidedly out of order here. Suffice it to say, that there are two entirely different schools of thought in regard to the method of treatment. In one, the opinion is that it is best to give large doses in a short space of time, preferably in one or two sittings. The other is that it is preferable to give small doses over a fairly long period of time. It has been my privilege to work with an exponent of the former technique and later to witness the application of radium in Professor Regaud's Clinic in Paris, where they strictly adhere to the second type of routine. In Vienna where what little knowledge I possess of this therapy was gained, Professor Simon administered a good sized dose in repeated intervals, usually from fourteen to twenty hours, at a sitting. His results over the period of the last five years have been uniformly good, notwithstanding the general belief that it is poor business to build up tissue resistance by repeated dosage. I soon realized why he followed this plan, for I noticed that when he could obtain the radium from the Institute for a longer period of time than that usually allotted, he made use of it to the limit. I must say that after visiting Professor

Regaud's Clinic in Paris and reviewing his results and statistics, it was brought home to me rather forcibly that Professor Regaud's technique and reasoning were assuredly the more practical, and in the application of radium I make use of his method.

It comprises the delivery of a high dosage (6000 mg. hr. up to 9000 mg. hr.) gamma radiation over a long period of time (six days) using highly filtered radium applicators distributed throughout the uterine and cervical canal, the lateral fornices and the cervix proper.

My 110 mg. of radium is distributed in capsules of fives, tens and twenties varying in length from 11 mm. to 17.5 mm., with outside diameter of 4 mm. and a wall thickness of 1 mm. The uterine capsules are 80 per cent gold and 20 per cent platinum while the filtration of the vaginal capsules is 100 per cent platinum. I have three sleeves with a thickness of 1.5 mm. platinum each, which are used inter changeably with the vaginal capsules, giving a filtration of 2.5 mm. of platinum.

It must be understood that in the radiation treatment of cervical malignancy, the lesion proper is not the factor of prime consideration. Resolution of a primary malignant lesion of the cervix uteri can be accomplished by the delivery of a relatively small dosage, but when low dosage is delivered the percentage of recurrence is high and the risk of spread of the disease ever present.

The purpose therefore of the high dosage of gamma radiation is not only to obtain resolution but to prevent extension, and, in order that this be accomplished, the high dosage must be delivered to the deep structures, not only to the tissues in the immediate vicinity of the applicators.

The reason for the use of heavy filtration (2.5 mm. platinum) immediately suggests itself if we bear in mind that when we use radium tubes, we are employing a source of heterogeneous gamma radiation; that is, gamma radiation whose wave length and penetrating power vary over a wide range. If we employ light filters, such as 1 mm. of brass, we are delivering to the tissues not only the hard penetrating gamma rays but a good amount of soft long-wave-length gamma radiation. This less penetrating radiation is absorbed by the tissues in the immediate proximity of the applicators and, if a fairly high dosage is delivered, a very intense reaction is produced due to the actual burning of those tissues in the proximity of the applicator. In this connection I may state that it is this type of "radium reaction" or "radium burn" that proved very discouraging to early investigators and is, at the present time, discouraging some workers using improper applicators. "Radium burn" is unnecessary and avoidable. A deep effect can be obtained, and by deep effect I mean the thorough and effective radiation of deep structures, by providing the radium tubes with sufficient filtration to absorb the long-wave-length gamma rays which would be otherwise absorbed by the layers of tissue in the immediate vicinity of the tubes. These tissues will therefore be protected and we can then proceed to deliver a high dosage without fear of overradiation.

One word about primary filters. Platinum is the filter of choice because of its high density. This is almost a direct proportionality. The density of brass is 8; that of silver 10.7; lead 11.0; gold 19.3 and platinum 21.5. Filtration of 1 mm. platinum is therefore equivalent to more than 2.5 mm. of brass. I will ask you to compare the filtration of 2.5 mm. of platinum ($21.5 \times 2.5 = 53.7$ density units), in other words, about 7 times as much filtration. We see, therefore, that when a dosage of 2000 mg. hr. is delivered by the introduction of a tube of radium filtered by 1 mm. of brass in the cervical canal, not only are we not making provision for the deep structures; but we deliver a higher dosage in the vicinity of the canal than with a 7000 mg. hr. dosage with good filtration and distribution.

Secondary filters must, of course, be used to take care of secondary beta rays from primary filters. The best combination of secondary filters is aluminum foil supplemented by ametal rubber. Ametal rubber is a special French rubber which contains no metallic element and gives off no caustic secondary beta rays. By using the primary and secondary filters which I have mentioned, we use pure gamma radiation.

It is superfluous to deal in detail with the technique of the application of the vaginal set-ups. I use seeds or needles to clean up an exophytic cervical growth and I amputate with a wire loop any large cauliflower protrusion. Douching and local treatment is usually necessary to reduce surface inflammation and discharge. The usual preoperative preparation of the vagina as for a simple dilating and curetting is all that is necessary prior to the insertion of the applicator. I emphatically state that Hanks or Hegars dilators should be used instead of the Goodell. The Goodell dilator traumatizes and lacerates the cervical canal tissues while the former give smooth graduated divulsion. I use the tandem arrangement of radium capsules in the uterus with a 5-5-10 mg. in a dead end ametal tube. In the vagina I make use of a pessary or colpostat with 10 mg. each in the fornices and 10 mg. before the cervix in a rubber barrel or a T tube. Packing the vagina tightly with as many 3 inch square gauze sponges as are necessary to fill it completely, I find to be infinitely better than using one yard or two yard packs. Immobility of the applicators is thereby guaranteed. Repacking on the third day is important with sterilization of the applicators and cleansing of the vagina before their re-insertion.

In closing, might I say that radium as a curative agency has been on trial for many years, and it is only recently that it has begun to come into its own. For a long time it has been correctly stated that women have refused operation for cancer of the cervix because they felt it was useless on account of the frequent early recurrence. The extensive successful use of radium within the last ten years should have eliminated this objection, but, nevertheless, the fact still remains that patients with this condition are presenting themselves too late for a cure to be accomplished. Aside from selfish reasons, it is a temptation to attempt treatment of each and every case which presents itself even though they are manifestly Group III or IV type. I confess that I have already begun to sidestep this type of inoperable cancer. I am attempting to use my radium only where I believe it will do good. We can keep our results in the highest per cent of apparent cures, and such success will do more for the future of radium than anything else. The attempt to treat these advanced cases with radium has had a tendency to bring this method into disrepute because the pain with which the late stages of the disease are attended, is believed by the laity to be due to radium burn. For this reason many patients refuse radium treatment. People expect too much, and one failure will undo the accomplishment of a dozen cures. If nothing else, may I finally emphasize the fact that *early* diagnosis and *early* radium treatment is of primary importance. If radium is to be used late in the disease, and *after all else* has failed, one must expect unfair criticism and poor results. Radium is not only *palliative*, it is curative.

MANAGEMENT OF UTERINE HEMORRHAGES

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CLEVELAND, O.

ONE of the problems most frequently confronting the physician is the management of uterine hemorrhage. The resources of the practitioner are frequently taxed to the utmost in the treatment of some of these cases.

Several questions arise when one sees a patient with uterine bleeding: (1) What is causing the bleeding? (2) What can be done to stop the bleeding?

This paper is based upon an analysis of 103 cases of uterine hemorrhages treated in private practice. In all these cases uterine bleeding was the main complaint, the symptom which caused the patient to seek medical advice. These patients were under observation long enough to observe the clinical courses of their disorders adequately.

There is enough of variety in this small series of cases to illustrate the management of the more frequent types of uterine bleeding. No attempt will be made to deal with the question of obstetrical hemorrhages.

Causes of Bleeding (Cullen).

A. Those dependent upon recent pregnancy
   1. Retained products of gestation
   2. Ectopic gestation

B. Those not dependent upon recent pregnancy
   1. Functional hemorrhage (hyperplasia of the endometrium)
   2. Pelvic infection
   3. New growths
      (a) Benign (fibromyomata, adenomyoma, endometrioma, polyps)
      (b) Malignant (carcinoma, sarcoma).

My 103 cases are divided as follows:

Retained products of gestation	35
Functional hemorrhages	26
Pelvic infections	20
Fibromyomata of the uterus	10
Carcinomata of cervix	8
Ectopic pregnancies	2
Uterine polyps	2
	103

RETAINED PRODUCTS OF GESTATION

This is the most frequent type of uterine bleeding seen by the physician. Many women with bleeding from this cause never consult a physician. Only the more serious and prolonged cases come to the attention of the physician. Curettage is seldom necessary following abortion or miscarriage. The uterus usually succeeds in evacuating its contents if given sufficient time. Then, again, the softened uterus can be easily punctured by injudicious handling of the uterine curette or sound. If the bleeding is brisk and relief of it is urgent it may be necessary to anesthetize the patient and dilate the cervix instrumentally; then insert the sterile finger into the uterus and attempt to remove the remaining secundines. One blade of the placental forceps may be used gently to curette the uterus. Very little harm can be done with this instrument if carefully used. Oftentimes just a small fragment of membrane or placental tissue is enough to keep up bleeding for weeks when it is retained in the uterus. When the uterus does not completely empty itself within a reasonable time it should be packed with a strip of sterile gauze, aseptic precautions being taken. When this packing is removed twenty-four hours later, frequently the remaining products of gestation come away with the packing. In some cases it is necessary to pack two or three times.

Usually no anesthetic is required for this procedure.

The less the interference in these cases the better it is for the patient. Many cases of pelvic infection can be traced to ill-advised instrumentation in these cases.

These patients should be put to bed and treated just as we would a postpartum patient. Ergot is given if indicated.

Of the 35 cases in this series only one required the use of the dull curette.

FUNCTIONAL HEMORRHAGE

There were 26 cases in this series classified as functional uterine hemorrhage. In these patients no gross pelvic lesions were demonstrable on pelvic examination.

In this group were 5 patients seventeen years of age, 4 nineteen years of age, 5 twenty-two years of age, 4 twenty-nine years of age, 5 thirty years of age, one thirty-two years of age, one thirty-four years of age, and one thirty-nine years of age.

The main complaint in each case was prolonged and excessive menstruation.

This condition is not uncommon at or near the menopause. When it occurs at that time it is very important to rule out cancer of the body of the uterus. Here a curettage of the uterus and microscopic examination of the material obtained will enable one to make the proper diagnosis. Cancer of the cervix would hardly be confused with functional hemorrhage, as the cervix is readily accessible to inspection and palpation.

Novak[1] and Cullen[2] have shown that in this condition there is hyperplasia of the endometrium. Novak[3] also states that corpora lutea are characteristically absent from the ovaries and that there is an increase in the process of follicular maturation and atresia in this condition of functional uterine hemorrhage.

Cullen advocates repeated curettage in these cases. Radium[4] and the *x*-ray are used. Hysterectomy[3] is required in some cases.

All of my cases were treated with corpus luteum extract. I have used the water-soluble extract hypodermically in 1 c.c. doses every day or every other day until the bleeding ceased.

Kaufman and Bickel[5] have recently reported satisfactory results in this type of uterine hemorrhage treated with corpus luteum extract.

If the bleeding is severe the patient is kept in bed. Seven of my patients required confinement to bed. Nineteen were able to come to the office for treatment. All of these patients responded promptly to the hypodermic injection of corpus luteum extract.

PELVIC INFECTION

Abnormal uterine bleeding occurs with great frequency in cases of pelvic infection. The bleeding is caused by ovarian pathology. I have often observed profuse bleeding with the passage of clots in these cases. Treatment of the infection often improves this condition. If the pathology is extensive enough surgery is required. I have taken up in detail the management of these cases in a previous paper.[6] Of the 20 cases in this series of pelvic infection causing uterine hemorrhage 10 required major surgical procedures. The others improved under conservative measures which included protein therapy, hot irrigations, rest in bed, corpus luteum extract, and cauterization of the cervix.

Uterine curettage is dangerous and of no value in these cases, as the bleeding is due to ovarian pathology.

FIBROMYOMATA OF THE UTERUS

These tumors are very frequent. Boyd[7] states that one in 5 women between puberty and the menopause have fibroid tumors of the uterus; that one in 2 or even one in one of colored women have them. All observers agree that these tumors are more frequent in colored than in white women. Cullen noted the presence of fibroids in 20 per cent of 742 women twenty years of age or over who came to autopsy at the Johns Hopkins Hospital between 1889 and 1906.[8]

All fibroid tumors do not bleed. Very large tumors may exist with no abnormal bleeding. The usual type of bleeding seen in fibroid tumors of the uterus is an increased and prolonged menstrual flow. The presence of a fibroid tumor postpones the menopause, and women past fifty years of age who menstruate regularly should be suspected of having fibroid tumors. The most profuse bleeding is encountered in the presence of submucous fibroid tumors. Even very small submucous tumors may cause profuse bleeding. Some of these tumors become pedunculated and present at the cervix as fibroid polyps. There is also intermenstrual bleeding in cases with submucous tumors. It is well to remember that in a given case of fibromyomata there may be subserous, interstitial, and submucous growths in the same uterus. The exsanguination in some of these patients is alarming, and transfusion is often required.

All the patients in this series were operated on. Other observers[9,10] report good results in selected cases treated with radium and the *x*-ray. The bleeding in these cases is so often due to submucous growths, so frequently are there adnexal pathology and intestinal adhesions, and in young women there is the danger of injuring the ovaries,[11,12] that I feel that surgery is preferable to irradiation in cases such as those just mentioned. In women at or near the menopause whose tumors are free and mobile, and who harbor no adnexal pathology, irradiation may be used to advantage. Large multinodular fibroids are best treated by surgery. The complicated intraligamentous growths which often interfere with the ureter are also best treated by surgery.

Finally, some patients who refuse to submit to surgical treatment will readily consent to irradiation.

CARCINOMATA OF THE CERVIX

I shall not attempt to elaborate on the management of these cases. Polak[13] states that the superiority of radium over surgery in the treatment of cervical cancer is now recognized by surgeons and gynecologists all over the world. I mention these cases because hemorrhage is often the first symptom observed by the patient, and is the cause of the patient consulting the physician. A thorough vaginal examination including speculum and bimanual examinations should be done in all cases of uterine bleeding. Further, no physical examination of a woman is complete without a thorough pelvic examination. Bleeding after the menopause should be considered a symptom of cancer until shown to be due to some other cause. Unless these cancer patients have their disease diagnosed early, treatment is of little avail.

Eight cases of carcinoma of the cervix have come under my observation in private practice during the period from April 30, 1926 to February 12, 1932. All of these cases were far advanced when first seen. Five of these patients had radium treatment; the others either refused treatment or died before treatment was instituted. One patient, in whom carcinoma developed in the cervix some years after removal of a fibroid tumor, lived four years after radium treatment was first given. One of these patients is still living, her condition having been recently discovered and treated. All of these patients were referred to competent radiologists for treatment.

ECTOPIC PREGNANCY

The management of these cases is surgical. Here diagnosis is very important. The type and character of the bleeding are of extreme significance. Usually in these cases there has been a period or two missed and this is followed by irregular bleeding. Not all cases of ectopic pregnancy present the classical picture of internal hemorrhage. Behney[14] suggests that cases be classified as obscure, non-urgent and urgent. Not infrequently, as in one of my cases, when the rupture is of some duration the case presents the picture of acute pelvic infection. The diagnosis between an old chronic pyosalpinx and unruptured

tubal pregnancy is sometimes very difficult; there may be irregular bleeding and a tubal mass in both conditions. Oftentimes laparotomy is required to solve the problem.

UTERINE POLYPS

In this condition there is irregular or continuous uterine bleeding and a leucorrheal discharge. It is usually the bleeding which brings the patient to the physician. Here a speculum examination is required to determine the source of the bleeding and the character of the lesion. Since many of these patients are in the cancer age, all the more emphasis should be placed upon a thorough examination. It is a great relief to both the patient and the physician when the source of the bleeding is seen to be a polyp, for this condition is curable by a simple operation. When the polyp presents itself at the external os it is an easy matter to grasp it with forceps and snare it off at its base with the tonsil snare. Cervical polyps are best treated by burning them off at the base with the actual cautery. In some cases it may be advisable to follow the removal of the polyp with curettage of the uterus. However, this should not be done in the presence of cervical or adnexal infection.

COMMENT

Uterine hemorrhage is such an ubiquitous symptom, intruding itself into almost every gynecological disorder, that an understanding of this manifestation is essential to the proper management of gynecological diseases. One might well say that if you understand uterine hemorrhages all things gynecological will be added unto you.

Thorough examination is a *sine qua non* in the management of these cases.

Many of our cases of pelvic infection and carcinoma of the cervix with their resultant bleeding and other symptoms could be prevented if more attention were given to the infected and lacerated cervix.

Bartlett and Smith[15] in a recent report state that in a follow-up study of 1700 cervices cauterized, not one of the patients is known to have developed cervical carcinoma.

Exact diagnosis is the key to the successful management of these cases.

SUMMARY

One hundred and three cases of uterine hemorrhages have been analyzed as to causation and treatment.

A proper understanding of the symptom of uterine hemorrhage is essential in the handling of many gynecological disorders.

The rare and less frequent causes of bleeding have not been included in this study because I have had no experience with them.

The measures used in treating these cases have been presented, and they have been satisfactory in my hands.

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CHOLECYSTECTOMY AND CHOLECYSTOSTOMY IN ACUTE SUPPURATIVE AND GANGRENOUS CHOLECYSTITIS*

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BY early operation in acute cholecystitis we determine the rapidity of the destructive process and correlate initial symptoms with the lesion and compare results with those obtained by medical treatment or delayed operation. Of especial interest is the influence of cholecystectomy on the morbid process. This subject, while being treated from the surgical viewpoint, is of interest to us all inasmuch as we see these cases either in the stage to be described or earlier. A thorough study of the condition may be of help to us in earlier cognizance of the existing condition and earlier eradication of the diseased organ.

As early as 1914 Dr. Babcock classified gall-bladder disease into three groups. This classification was made to facilitate study and treatment and is useful in any discussion of the condition. These stages are: (1) The stage with inflammation of the gall bladder previous to stone formation usually occurring between the ages of twenty to thirty and pathologically characterized by a catarrhal inflammation in the wall or mucosa of the gall bladder. These subjects have symptoms of epigastric distress, with belching, and a feeling of fullness after meals. Patients with prolonged inflammation have mild attacks of epigastric and right hypochondriac pain. (2) The stage with stone formation, and obstructive symptoms characterized by attacks of colic and severe epigastric symptoms, qualitative dyspepsia, etc. (3) The stage of terminal complications including the cases of empyema, gangrene, or perforation of the gall bladder. In this stage there are usually necrosis of the wall, pericholecystitis, liver changes and often cardiac involvement.

Chronic cholecystitis has been very carefully studied both as to diagnosis and treatment but it is the complication group that needs elucidation. Before we discuss those cases a very brief review of the subject seems in point. In touching on the etiology of this condition which we call the third stage of gall-bladder disease, we see that it is usually the result of neglected first and second stage disease with resultant complications. The patients are usually above fifty years of age, 85 per cent are women, and too often they have symptoms of cardiac or hepatic disease. Their history is nearly always the same, i.e. years of abdominal distress, with epigastric discomfort after meals, gradually becoming worse. Later they have developed violent attacks of pain, at first often not so frequent but finally very severe, transient, usually nocturnal in type, and nearly always requiring an opiate to relieve them. They have often had several of these attacks, but following the administration of the narcotic they have had prompt relief and have continued their life as before. Gastric discomfort from heavy food and the qualitative dyspepsia have persisted between the attacks, however. Eventually the patient may have an attack which is much more severe than the preceding ones, and unlike the others persists and is not relieved by morphine even in large doses. The severity of this attack drives the patient to the hospital.

The pathological condition varies with the length of time that the process has

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been going on, the severity of the attack, the type of complication, and the infecting organism. Most often we find a stone occluding the neck of the gall bladder or, less frequently, the cystic duct. With its outlet obstructed, the gall bladder enlarges from the entrance of serum and mucus, the wall and mucosa become greatly distended, and the tension causes an ischemia of the wall and a subsequent beginning necrosis. This is followed by the entrance of leucocytes and blood cells and later, the presence of gross pus. The process is largely mechanical, a necrosis due to pressure but a streptococcus of low grade virulence is often present, which may be difficult to cultivate. In a smaller percentage of cases the sepsis is caused by the colon bacillus and here foul pus is encountered. In these cases the infection is much more serious and recovery is effected in only a very small percentage. The organ containing pus mixed with thick mucus, disintegrating blood and necrotic mucosa is usual, and it is with this condition that we are most concerned. With delay, the necrosis may extend through the wall of the gall bladder with perforation. This results in a localized peritonitis and pericholecystitis or generalized peritonitis. Often the liver will show changes, the most serious of which is liver abscesses. Escaped stones may be walled off by peritoneal adhesions. Chronic hepatitis is almost invariably present. There may be other changes, such as stones in any part of the common duct or ampulla of Vater, malignancy of the gall bladder, its duct or head of the pancreas. With this brief introduction into the etiology, symptomatology and pathology of the condition we are prepared to discuss the cases reviewed at this hospital.

In the last thirteen months at The Temple University Hospital, 130 patients have been admitted to the Surgical Service of Dr. W. Wayne Babcock. Of this number. 120 have come to operation, 45 being in the third or terminal stage. This percentage of 23.4 is a large one. Of the 45 cases of gangrenous or purulent cholecystitis, 42 patients (91 per cent) entered following an acute attack of pain and colic. The other 3 patients complained of mild pain in the right upper quadrant. Of these 45 patients 40 were operated on within twenty-four hours after admission to the Surgical Service. Five were studied or prepared from one to five days before operation. Thirty-five of the patients recovered and ten died, a mortality rate of 22.2 per cent. Twenty-three (52 per cent) had cholecystectomy performed on them and all recovered. Twenty-two patients had cholecystostomy and of these ten died, a mortality for cholecystostomy of 45.5 per cent. This mortality, while alarmingly high, is not as significant as it appears at first. The patients in the more serious condition were selected for cholecystostomy as will be shown later.

All but one of the gall bladders contained stones and in this one there had probably been a stone before as there was a history of colic. The number of stones varied from one to 480 present in one gall bladder. The gall bladder condition was classified as empyema in 21 cases, early purulent in 9, and gangrene of the wall in 15. Three of the latter gall bladders had perforated. In 2 of the 3 perforated cases the patients recovered, the third died of peritonitis. Cholecystectomy was performed in 9 empyema cases, 9 of the early purulent cases, 5 of the gangrenous, including one of the perforated cases, all with recovery. The rest of the patients had cholecystostomy.

An analysis of the deaths is of interest to us as perhaps throwing light on the high mortality figure. We expect to find peritonitis as the greatest cause of death and this was so in 6 of the cases. So often in reports from clinics the cause of death is given as pneumonia or some cardiac complication which was, in reality, terminal after a generalized peritonitis. Many of these patients here registered had limited or complete autopsies so that in nearly all the correct cause for the death

of the patient is known. One of the patients who died of peritonitis had a pulmonary tuberculosis which no doubt weakened the resistance and hurried the death. Another patient showed a pancreatic abscess secondary to the original gall-bladder disease which had ruptured and caused the fatal peritonitis. A third had multiple liver abscesses and was, of course, quite late. One other patient had nephritis as a contributing factor, although the death was peritonitic. A fifth had a terminal pneumonia. All of these factors were but additional and cannot blind us to the fact the peritonitis was the actual cause of death. Hepatic insufficiency, a misunderstood and often unrecognized entity, is undoubtedly a contributing cause in those deaths classed as peritonitic, and one patient had perhaps one of the so-called liver deaths as C. G. Heyd so aptly puts it. In the deaths other than peritonitis, there were two actually cardiac. One of these was apparently a coronary accident about eight hours after operation at a time when the patient was doing exceptionally well. The other cardiac death was in a patient who had aortic heart disease of some years' standing, and decompensated following operation. Despite stimulation she did not respond, dying in about forty hours after operation. One patient developed the very severe and fatal complication of complete anuria. Attention to this factor has recently been brought to the notice of the profession by Dr. Willard Bartlett, Jr. of St. Louis who reported 5 cases after biliary operations, in which all of the patients died. In our case the patient passed only 3 oz. of urine in the first forty-eight hours after operation and after a great deal of stimulation, the kidneys slightly opened but with a creatin of over six the patient's condition was irremediable. She died in acute uremia on the fourth postoperative day. In Bartlett's cases each fatality from anuria was in a case associated with jaundice and he attributed it partly to the jaundice. Our patient was not jaundiced and differs in this respect. As far as known there was no definite kidney disease previous to operation although there was some cardiac myotonia and perhaps an associated low grade nephritis that did not show itself in the blood pressure or urine analysis. It is of interest to show that all the known kidney stimulants such as glucose, the niters and alkalies, venesection and even a very small dose of salyrgen had no effect in this case. A continuous venoclysis of 2 per cent glucose after the method of Hendon did cause a little more urine excretion on the third day, but probably was of more harm than benefit as it helped to overload the circulatory system. One patient lived fifty days following cholecystostomy for an obstructed common and cystic duct, being kept alive by multiple blood transfusions for the three weeks that a localized peritonitis threatened to kill her. She then did well for about two weeks and her abdominal condition entirely cleared. A pneumonia then added to our difficulties and this gradually spread to involve all five lobes of the lung and was the actual cause of death. In summary of the deaths let us say again that 60 per cent died of peritonitis, 10 per cent of uremia, 10 per cent of pneumonia, and 20 per cent of cardiac complications.

Table 1
CLASSIFICATION OF CASES AS TO AGE

Age in Years	Cases	Per Cent	Cholecystectomy	Cholecystostomy	Mortality	Mortality Per Cent
20–30	1	2.2	1	0	0	0
30–40	10	22.2	6	4	1	10
40–50	9	20.0	6	3	0	0
50–60	12	26.6	8	4	2	16
60–70	12	26.6	2	10	6	50
Over 70	1	2.2	0	1	1	100

In choosing the operation to be used in these cases, one is guided more by the age of the patient and the condition of the other organs than by the pathological condition of the case in point. Naturally in this series of cases, the operation of cholecystectomy was performed on the better patients. The age shows this quite well. The average age of all patients operated on was 54.1 years. The age average of the subjects that had cholecystectomy was forty-six years. The age average of the ones who died was 61.4 years, a difference of nearly fifteen years. In some cases there was a question as to the patient living through the procedure, so the simplest operation was chosen. Most of the patients (37) were operated on under spinal anesthesia. On 8 patients in very bad condition another anesthetic was chosen: ethylene in 4 and local alone in 4. The choice of an anesthetic is of course an individual problem, but where the condition of the patient will warrant its use, spinal anesthesia makes for technical ease at operation and therefore for better operation.

Until recent years the teaching of nearly all clinics was to perform the operation of cholecystostomy whenever pus in the gall bladder was encountered. The tendency now is to do this operation only when it is impossible to do the better operation of cholecystectomy. Mentzer tells us that at The Mayo Clinic in 1906 the percentage of cholecystostomy was 58.7 while in 1926 the percentage was 4.3. In selected cases the mortality will not run high, as this small series tends to show. It is, of course, technically more difficult to perform a cholecystectomy in the presence of a gall bladder distended with pus. There is a mental and physical hazard present at all times and this may tend to make the operator hurry to get it out instead of taking more time and consequently more care. Where the gall bladder can be removed without draining off the pus, the prognosis will be definitely better. This is often quite difficult to do as it is harder to handle and, as previously stated, the mental hazard is great. It is worth a trial however, dependent on the operator's technical equipment and the condition of the patient. Even where the gall bladder must be first aspirated, the aspiration point can be closed with a clamp and the cholecystectomy continued as before. This series of cases would tend to make one think that the operation of cholecystectomy is not as fraught with danger as we have been led to believe. In a selected group this seems to be true. Many of the patients who had cholecystectomies in this series were elderly, 25 per cent being approximately sixty years of age, which shows that older people can stand the more severe operation. For patients in poor general condition, as for example the fatal ones here presented or where the cholangitis requires the use of the gall bladder for drainage, one would not advocate more than the palliative operation; however, we must remember that it is only a makeshift operation and that the complications are many and the mortality quite high. The economic side of the question, while of secondary importance, is worthy of note. There is a definite saving in hospital days by the cholecystectomy operation. In this series it was found that the average length of time in the hospital after cholecystectomy was nineteen days, while in the drainage operation, the average time was twenty-six days. An average saving of one week is thus realized. The effect of age and general condition again plays its part in this consideration, but where the weeks of drainage are eliminated, there is no doubt a great deal of time saved, both for the patient and the hospital. It might be summed up as follows: If the patient is able to stand only a quick limited procedure, perform cholecystostomy, remembering that it is often only palliative; if the patient can stand an operation fairly well do a cholecystectomy and make this rather than the disease condition the factor for the differentiation.

Another great problem that we must meet in these cases is that of neglect. Twenty-six, or well over 50 per cent, of these patients gave a history of colic attacks of great severity for from one to fifteen years before. Only 8 stated this was the first attack of pain of the stone type. All but 5 gave a history of years of dyspepsia before, indicating the passage through the first and second stages.

TABLE II
NUMBER OF YEARS OF ATTACKS IN RELATION TO DISEASE CONDITION AND MORTALITY

Length of Attacks	Early Purulent	Empyema	Gangrenous Necrotic	Total	Deaths	Mort. Per Cent
Sudden onset....	2	4	2	8	0	0
One year or less...	4	4	2	10	1	10
One to two yrs..	1	3	3	7	2	28.2
Two to three yrs.	1	0	4	5	1	20
Three to four yrs..	1	1	1	3	2	66.6
Four to five yrs..	0	2	0	2	0	0
Five to eight yrs.	0	3	1	4	1	25
Over eight yrs.	0	4	2	6	3	50
Totals...	9	21	15	45	10	22.2

Thus it would appear that most of these patients were neglected. We now know that except in rare instances all cases of this type should have had an operation before they became terminal. The relation between the years of attacks and the mortality percentage is striking. The mortality correspondingly rises with the number of years of attacks. Whereas in operations on patients with a history of less than one year of colic only 10 per cent died, in patients with a history of attacks for eight years, 50 per cent died. Age plays its part in this result but is again an additional argument for earlier interference. The damage to the heart, liver, and kidney has been done in these elderly people. Many years ago, Dr. Billings and Dr. Robert Babcock of Chicago pointed out the connection between gall-bladder disease and the heart disease, showing that the removal of the diseased gall bladder allows some of the hearts to recover and stops further myocardial degeneration. Dr. Billings was one of the first to have the operation of cholecystectomy performed for heart disease, presenting himself and his cardiac involvement as a practical demonstration of the value of the procedure. These patients often have been handled by their doctors at home on diet without much relief for years. They have been carefully guided through stone colic attacks with morphine, often each attack becoming more severe. In the acute condition time and money is wasted on gall-bladder *x*-ray study, a procedure doubtfully diagnostic at any time and quite useless in acute cases. So often delay is decided upon because the roentgen ray shows no calculi. In an edematous thickened organ in which no dye can possibly enter, the stones are masked. Even today it is sometimes forgotten that stones are the late result and not the cause of gall-bladder disease.

That the practice of holding the patient at home or in the hospital, either for further study or for localization, will reflect in the mortality is shown by the fact that in these registered deaths, all but one were temporized with from eight to thirty-nine days and in the one in which there was no delay, the death was a cardiac accident. The average number of days that the fatal cases were held before operation was thirteen. Where cholecystectomy was performed the average delay was eight days.

Inasmuch as even in the early cases here presented the patients had pus in

the gall bladder, we must admit that the reaction of the organ to the process is an individual one. However, where the operation was performed within forty-eight hours after the onset of the colic, the mortality was nil and the morbidity much less, with fewer hospital days. This fact emphasizes again the fallacy of waiting for a more opportune operation time as in the delayed cases there was no abatement of the disease process and the operation was performed as a final emergency when the patient's condition was very poor.

This condition does not allow for procrastination. The general practitioner must be educated to the fact that any attack lasting more than two hours requires surgical interference. He has been taught that there is no such thing as an emergency gall-bladder operation and that the patient should be held until the acute attack has subsided. In some early cases this will be successful but in such cases as we are presenting he is merely delaying a necessary procedure while allowing the general condition to become worse. Where gangrene has set in, the process will not stop and the inevitable result will be perforation, either into the peritoneal cavity or a neighboring viscus, usually the liver. With the gall bladder distended with pus there is a migration through its wall of infecting organisms and the beginning of a local peritonitis even before rupture. With the onset of the gangrene, the clinical picture, as in appendicitis, improves. The pain lessens, the rigidity or tenseness of the abdominal wall relaxes, and the patient generally feels better. This is but the calm before the storm and our mortality will rise with every hour of delayed operation from this time on.

One wonders whether in the next few years, the patients with suppurating gall bladders will have to suffer the same fate that the ones afflicted with acute appendicitis suffered in the past while the medical profession floundered helplessly with the problem of early or delayed surgery. The parallel to acute appendicitis is rather close. The policy of immediate operation on appendicitis is not an old one, and it is to be hoped that the toll of life necessary to make appendectomy the corollary of acute appendicitis will not have to be repeated to make early surgery the treatment of these third stage cases. When one has seen the tightly distended, white, edematous gall bladder with the beginning plastic exudate on its outer coat, it is impossible to picture it subsiding so that a more favorable time for surgery will be presented. It is significant and worthy of emphasis that in a series of 45 purulent gall bladders, with the exception of the cardiac accident, no death occurred where the operation was performed within nine days of the onset of the terminal attack, despite the fact that cholecystectomy was performed in over half. Let us again repeat, there can be no procrastination.

The mortality in clean operations on the gall bladder is not high. Dr. Judd at The Mayo Clinic gives the very good figure of 1.7 per cent and a gross Mayo Clinic mortality of 2.8 per cent in 16,980 cases, a very safe margin for one to work on. Dr. Lahey at Boston has a mortality of 2.2 per cent and he adds the additional surgery of routine exploration of the common duct, not by palpation but by vision or the introduction of a scoop into the duct. The mortality of clean cases of cholecystectomy at this Clinic runs in this neighborhood. This argues so seriously in favor of early operation that one should no longer wait through repeated gall-bladder attacks without referring the patient for operative eradication of the diseased organ. The liver suffers more than any other organ. Liver abscess gives a very high mortality and chronic hepatitis and liver cell damage shorten life. This problem is being studied in England as evidenced by the excellent article on Surgery of the Biliary Tract written this year by R. P. Rowlands, Surgeon to Guy, Hospital, from whom I quote:

"It is a great mistake to let many recurrences take place, to allow time for dangerous complications to develop leading to much suffering and a greatly increased mortality from delayed operation."

The gall bladder is not an essential organ as shown by the fact that certain animals such as the horse, deer, rat, etc., function well without it. Once diseased, the gall bladder quickly becomes functionless. Dr. Eliason recently reviewed 100 cases of cholecystostomy on Division c at the University of Pennsylvania Hospital and found that only 1 of 20 was functional one year after operation and that those that were definitely found diseased at operation never regained function. It is interesting to note the results published by The Mayo Clinic this year on their follow-up work on biliary disease. Good results were obtained in 84 per cent of the cases after cholecystectomy while there was a cure in less than 60 per cent of the cases after cholecystostomy. This was true whether there were stones present or not. This is in line with our findings here, as 4, or 18 per cent, of the 22 patients treated by cholecystostomy have already returned to this Clinic in less than a year for treatment of their previous condition.

In the future it is believed that we will see more and more the trend to earlier and more thorough surgery and perhaps the gradual decrease in the percentage of the terminal stage of gall-bladder disease with its high mortality and resultant damage to the parenchymatous organs.

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GALL-BLADDER DISEASE

ONE THOUSAND END RESULTS*

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IN this study of personal cases of gall-bladder disease exclusive of cancer it was sought to tabulate 1000 results one year or more postoperative. This involved a study of approximately 1500 histories antedating January 1, 1931. The immediate results were also studied and are epitomized in table 1 which shows the character of the operation, whether done in the stage of acute or chronic inflammation, with the number of recoveries and deaths, and the mortality percentage.

There is a lot of food for thought in these figures. Note the tremendous difference in mortality in favor of operating in chronic inflammation rather than in acute. Note the better immediate results in inflammation limited to the gall bladder compared to the results when the disease has involved the ducts.

In 1916 the author stated as the result of microscopical studies of a series of 100 cases that gall-bladder disease is a chronic progressive inflammation and that its treatment should be early cholecystectomy *whenever continued, repeated or disabling symptoms occur.* Time and further experience have not changed my views. This should not be interpreted to mean that every patient in whom a diagnosis of gall-bladder disease is made should be operated on for in many instances the disease does not cause continued, repeated or disabling symptoms. It is estimated that of every 100 cases 80 either become quiescent or present such minor disturbances as not to interfere very much with the patient's well-being and therefore do not require surgical intervention. Of the remaining 20 there are perhaps 15 in whom operation is distinctly indicated and 5 in which it is a question of judgment as to whether or not operation should be performed.

TABLE 1
OPERATIONS: IMMEDIATE RESULTS

	Cases	Recovered	Died	Mortality (Per Cent)
CHOLECYSTOSTOMY				
Acute	235	205	30	12.8
Chronic	17	17	0	0
	252	222	30	11.9
CHOLECYSTOSTOMY AND CHOLEDOCHOSTOMY				
Acute	7	6	1	14.3
Chronic	5	5	0	0
	12	11	1	8.33
	264	233	31	11.7
CHOLECYSTECTOMY				
Acute	278	260	18	6.5
Chronic	589	578	11	1.9
	867	838	29	3.33
CHOLECYSTECTOMY AND CHOLEDOCHOSTOMY				
Acute	19	14	5	26.3
Chronic	30	30	0	0
	49	44	5	10.2
	916	882	34	3.7
CHOLEDOCHOSTOMY ALONE				
Acute	6	4	2	33.33
Chronic	11	9	2	18.2
	17	13	4	23.5
CHOLECYSTOGASTROSTOMY				
Chronic	2	2	0	0
CHOLEDOCHOGASTROSTOMY				
Chronic	1	1	0	0
CHOLEDOCHOPLASTY				
Chronic	6	4	2	33.33
	1206	1135	71	5.9
Ops. in acute cases	545	489	56	10.3
Ops. in chronic cases	661	646	15	2.3
	1206	1135	71	5.9

* Read before the Medical Society of the County of Kings, May 17, 1932.

If latency could be brought about by diet, medication or treatment other than operation it would of course be preferable.

Let us take up very briefly from the surgical standpoint what gall-bladder cases may be treated without operation. Medical treatment is indicated in all acute inflammations of the gall bladder showing a tendency to subside with the exception of acute cholecystitis with gangrene, perforation, empyema and cholangitis. Medical treatment is also indicated in all chronic cholecystitis cases which tend toward latency and in hydrops of the gall bladder and in cholecystitis cicatrans not giving pain. Why is medical treatment indicated in these acute and chronic inflammations? In the acute because they are temporary and in both acute and chronic because they are not disabling, do not give the patient much discomfort and do not interfere to any great extent with his enjoyment of life nor his ability to earn his living.

Operation is indicated in acute cholecystitis which does not subside quickly, cholangitis both acute and chronic, gangrene of the gall bladder, perforation of the gall bladder, beginning carcinoma of the gall bladder, in all cases of chronic cholecystitis, of which there are many forms, in which health is affected over a period of time either through recurring attacks of pain or which cannot be brought to a degree of latency which permits of comfortable digestion and the pursuit of livelihood without too much interference.

There are two classes of cases: those in which operation must be done at once in order to save life and those in which we have time to consider whether operation is advisable or not. In the first it is the physician and surgeon who must throw the weight of their experience in the balance to cause the patient to decide and must insist upon an immediate operation. In the second class there is time in which the case may be studied, discussed with the patient and a mutual decision arrived at in accordance with the degree of interference with the patient's comfort and livelihood.

In the first class are the cases of acute cholecystitis not rapidly subsiding, the cases of seropurulent chronic cholangitis, acute cholangitis, gangrene of the gall bladder and perforation of the gall bladder. In the second class are the cases of beginning gall-bladder carcinoma and the cases of chronic cholecystitis in which the patient's comfort and livelihood are being materially affected. I think that all physicians and surgeons can agree with this classification. Certainly in the first group we can all agree as these septic conditions are a direct and immediate menace to life. In the second group it is really up to the patient to give the final decision. He knows and he alone knows how much interference there is with his comfort and livelihood. We can, however, lay before such a patient his probable chances for cure or at least for the decided amelioration of his symptoms by operation and also the mortality of such an operation in skillful hands.

In many cases it will happen that in spite of recurring disabling symptoms the patient will so dread an operation as to refuse it when the attack has once subsided. Unfortunately for these patients their chances of recovery and of cure following operation are greatly enhanced if the operation is done between the attacks at a time when the minimum of inflammation is present, when they feel quite well and free from symptoms. If such patients are operated upon during an attack at a time when they will more readily submit to operation on account of their desire for relief of pain we cannot, in many instances, do a radical operation which will almost certainly relieve them, but must content ourselves on account of technical difficulties and dangers in doing a drainage operation, thus leaving a gall bladder which, in at least 25 per cent of the cases, gives subsequent trouble. Frequently if it is explained to the patient that an operation between the attacks minimizes the possibility of a second operation the patient will

more readily submit. If, however, the patient will only submit during an acute attack then it is again up to the physician to decide whether such an operation should be performed. In this decision he will be aided by a study of the history as to the degree of discomfort and disability. We hesitate to make an emergency operation of such cases because we know much better a result can be achieved between attacks. Here let me interpolate a word of warning. The inflammation of the acute attacks does not subside as quickly as the subsidence of the symptoms indicates. I have operated three or four weeks after the subsidence of all symptoms and have still found a very considerable amount of inflammation, so much so as to make ideal cholecystectomy of more technical difficulty than one would imagine. It is better to wait six weeks after a severe attack before operating if the condition of the patient will permit. It is certainly not waiting a sufficient time to operate a few days following an acute attack as is the custom so often in our hospitals. Our objective should be to lower the mortality of gall-bladder surgery to a point that will approximate the true mortality of the disease itself and by so doing convince our medical friends of the advisability of early operation.

In the cases in which we advise operation we base our advice on the degree of discomfort and interference with the patient's pleasures, comfort and livelihood. The symptoms need not necessarily be severe nor necessarily colics, they may be more in the nature of pressure sufficiently painful to aggravate the patient and to keep him from doing his work properly. Many such patients continue to work but their efficiency is impaired. Where patients present symptoms of nagging discomfort they should be advised that operation will cure or at least relieve them to a great extent. As a matter of fact patients presenting these symptoms between their acute attacks become worse and worse the longer they delay and finally must come to operation. The earlier the operation is done the better for them.

A proper knowledge of gall-bladder disease would enable the physician to send such cases to the surgeon at a time when operation is practically without danger. Cases discussed by the physician and the surgeon will do much to help them both to properly care for this disease.

The presence or absence of symptoms cannot always be properly interpreted. There are cases which have no tenderness at all in the region of the gall bladder and yet at operation the interior of the gall bladder shows marked acute inflammatory changes which would undoubtedly have led, in a few days, to perforation. Nor can clinical symptoms always be depended upon. Many cases of empyema show slight or no fever; many stones in the common duct show no jaundice.

Pain is one of the indications for operation, more so when recurring repeatedly and becoming more constant and especially when of a pressing character. It is usually the pain which causes the patient to consult the surgeon. More or less constant pain is practically always a symptom of chronic inflammation, but chronic inflammation does not always give pain. Some cases without pain show empyema of the gall bladder and some chronic cholangitis, in both of which operation is indicated.

Jaundice and enlargement of the liver are indications for operation just as pain is when the conditions are of a chronic character. In spite of the extensive studies in gall bladder pathology there are physicians who cannot understand how the patient can have gall stones without jaundice. An acute attack of jaundice is not an indication for operation unless it appears coincidently with symptoms of acute inflammation. In the latter case the jaundice depends on involvement of the lymph glands around the head of the pancreas and along the common duct. In the majority of cases with acute jaundice the jaundice is caused by pressure on the common duct or acute closure of the duct.

When a sudden closure of the duct is caused by stone there is an accompanying acute choledochitis. If the inflammation goes on to suppuration or becomes chronic jaundice will persist. In such cases operation should not be delayed. Early operation in cases of chronic closure of the common duct shows a mortality of 3 to 4 per cent; delay increases the danger threefold. In chronic cholangitis jaundice and colicky pain may disappear and chills and vomiting occur. The temperature may range as high as 104° F. Operation should not be delayed. It is useless to wait for the obstruction to be overcome by other than operative measures. There are occasionally reported cases with chronic closure of the common duct in which recovery has occurred without an operation. The quiescent period can only be temporary; the inflammation has subsided and the stone is resting. Sometimes the stone passes through the papilla or finds its way into a neighboring organ through ulceration. Though this occurs in a few cases and is Nature's attempt to cure it is unsafe to wait for such an event. Early operation gives a much lower mortality.

Some physicians rely upon the physical examination to give indications for operation. This is not always satisfactory; the history is what we depend upon most though in certain cases the physical examination is of decided value as in the following instances:

1. An enlarged gall bladder not sensitive to pressure without jaundice. Is operation indicated? No. Why? Because such a condition is almost always a sterile hydrops of the gall bladder which is harmless.

2. An enlarged non-sensitive gall bladder with jaundice. Should such a case be operated upon? Yes. Why? Because such a physical finding is usually carcinoma of the gall bladder, duct or pancreas, or a chronic pancreatitis. In such cases operation (cholecystenterostomy or cholecystogastrostomy) can in the case of cancer often relieve and if the case is one of chronic pancreatitis the operation may really prove curative.

3. An enlarged gall bladder with slight jaundice and with the gall bladder slightly sensitive to pressure. Should operation be done? Yes. Why? Because as in the second instance cited such a condition is usually one of carcinoma or chronic pancreatitis.

4. A very tender and well-circumscribed enlargement of the gall bladder with little or no jaundice. Should operation be done? Yes. Because such physical findings point to an inflammatory process of a seropurulent nature. Operation in such cases is not so urgent but still an operation must be done. When it is done early the mortality in such cases is about 3 per cent, and the mortality is increased by waiting. The operation is not so emergent as in:

5. A case presenting the same symptoms and clinical appearance as are present in gangrenous appendicitis except as to the location of pain which is in the gall-bladder region and in which there may be only a little resistance over the gall bladder. Should operation be done in such a case? Yes. Why? Because these symptoms are those of gangrenous inflammation and while no tumor can be felt either because of the thickness of the abdominal wall, the location of the gall bladder under the ribs, or the primary rigidity of the abdominal wall yet the sudden subsidence of the local symptoms leads us to suspect gangrene or perforation. Here the clinical appearance does not at all denote the serious pathological changes but operation is most imperative. Usually gangrenous cholecystitis is readily diagnosed and should always be treated in the same manner as gangrenous appendicitis, acute pancreatitis or strangulated hernia, that is, by immediate operation.

6. Cases in which sensitiveness to pressure in the gall-bladder region persists; not only the sensitiveness felt by the patient but also the increased sensitiveness caused by the examining hand. This is very important. Should operation be advised? Yes. Why? Persistent sensitiveness

is the main indication for operation. The area of sensitiveness varies according to the location of the gall bladder. Cases in which the gall bladder can be mapped out and in which not only it is sensitive but the surrounding peritoneum is sensitive and in which the sensitiveness persists are cases of acute purulent cholecystitis. The differentiation between this and perforated duodenal ulcer is largely made on the area of sensitiveness but such a differentiation is not necessary. Both conditions require immediate operative interference.

7. Cases in which the patient complains of continuous pressure in the gall-bladder region with a tender gall bladder, the patient not being able to attend to his daily duties and deprived of enjoyment of life through the continuance of the pain. Should operation be done? Yes. Why? Because such a condition is disabling. When we operate we find changes in the gall bladder which can only be corrected by operation.

8. Cases where jaundice appears in which there is one chill and rise of temperature but in which a gall-bladder tumor is not present and in which sensitiveness is lacking. Should operation be done? No. Why? Because such a condition may be one of simple cholecystitis which may readily subside, but if fever and chill recur or if persistent sensitiveness be added operation should be advised at once.

9. Cases showing enlargement of the liver. This of itself is not an indication for operation but a liver progressively increasing in size with fever and severe constitutional disturbances, with or without jaundice, in a patient who has a history of gall-bladder disease, is an indication. These physical signs and symptoms point to suppurative cholangitis, a disease in which medical treatment is only palliative but in which early operation, free drainage of the infection by choledochostomy, is the only means by which life may be saved. To delay is fatal. Medical measures, sodium salicylate combined with urotropin, are helpful as adjuvants to surgery. The subject of enlargement of the liver in relation to gall-bladder disease requires more consideration than is allowed for in the space at our disposal.

10. Cases showing enlargement of the pancreas in the course of gall-bladder disease but in which the gall bladder is not palpable. Should such a case be operated upon? Yes. Why? Such a case is either one of acute inflammation of the gall bladder with subsequent involvement of the pancreas through the connecting lymph glands or a case of cholangitis, both conditions which demand operation. It must be remembered that pancreatic involvement occurs in about one-half of the cases of cholangitis and in about 10 per cent of cholecystitis cases, though in the latter the pancreatitis may only be discovered at operation.

11. Cases presenting jaundice. When is jaundice an indication for operation and when does it contraindicate operation? Patients with jaundice who show a fairly widespread bleeding under the skin and who show acidosis should not be operated upon without proper medical preparation. Slight jaundice which may be from pressure of lymphatic glands along the common duct or about the head of the pancreas or beneath the liver does not increase the danger of operation. Jaundice caused by chronic closure of the common duct operated upon early does not materially increase the danger. In this class of cases we should not wait until slight jaundice progresses to severe jaundice with its bad effects upon all tissues and organs including the blood. It is quite important that we operate at the right time. Many cases are brought to us late in the course of the jaundice. It has long been taught that to operate during jaundice is extremely dangerous so that the patient is not apt to consult the surgeon unless urged to do so by his physician, thus delaying operation until it is too late. Unfortunately cases of jaundice are rather difficult to prognosticate. Often catarrhal jaundice with its accompanying gastroduodenal catarrh and

its mucous plug in the common duct is confused with chronic pancreatitis, tumor of the head of the pancreas, a tumor growing retroperitoneally either involving or pressing upon the common duct secondarily or with stone in the common duct. The usual course of catarrhal jaundice is six weeks. Under modern medical treatment (duodenal drainage) the course of the disease is shortened one-half. If a case has been diagnosed and is being treated as one of catarrhal jaundice in which no other diagnosis is possible and the jaundice persists beyond the three to six week period operation should be performed. Catarrhal jaundice is jaundice free from pain. In such cases duodenal drainage is advisable to shorten the period of the jaundice. When pain is present or when pain has been part of the previous history or when pain develops during the course of the jaundice operation should be done immediately. The earlier the operation is done in the course of the jaundice the safer the operation.

The size of the gall bladder is of value in differentiating between pressure of malignant disease and stone in the common duct as a cause for the jaundice. If we find the gall bladder distended and jaundice present we make a provisional diagnosis of carcinoma. We are not, however, always able to palpate the gall bladder on account of other factors so that while the presence of a palpable distended gall bladder is of value its absence is not of such important diagnostic significance. In catarrhal jaundice the gall bladder is flabby and not enlarged.

Frequently jaundice lasts only a few days. In such cases there is a history of pain followed by sudden jaundice rapidly clearing up. Here we have to do with a stone which has passed from the gall bladder to the duodenum, though in certain cases it may remain in the common duct quiescent for a while only to cause trouble later. One such attack is not sufficient indication for operation. Frequently such cases go for years without subsequent trouble. When the attacks are repeated and disabling, however, operation should be done.

Before leaving the subject of jaundice let me impress upon you that jaundice is not a necessary symptom of gall-bladder disease. The majority of cases never have jaundice. When present, except when evanescent, operation should be done early no matter whether the jaundice is caused by an acute lymphadenitis, by choledochitis, by stone, by sclerotic pancreatitis or by carcinoma of the pancreas or common duct. No matter how skillful we are in diagnosis we cannot always be sure of the exact pathological conditions present and to delay operation in the presence of jaundice, unless the case is one of catarrhal jaundice or familial jaundice or infectious jaundice (Weil's disease) or hemolytic jaundice, is to invite disaster. Jaundice persisting following a slight attack of cholecystitis should be an indication for immediate operation. Jaundice is only one of the symptoms. It may accompany acute cholecystitis as well as chronic cholangitis. The depth of the jaundice is of value in arriving at a probable diagnosis. Jaundice caused by stone is apt to be deeper and more bronze than that caused by pancreatitis which is lighter and more yellowish green. Variable jaundice with a gall bladder which is not palpable makes a diagnosis of intermittent closure of the common duct by movable stone plus inflammation probable. Painful enlargement of the gall bladder with jaundice makes a diagnosis of cholecystitis with lymphadenitis probable. Painful enlargement of the gall bladder which rapidly disappears suggests a diagnosis of cholecystitis which has drained through the common duct. Jaundice coming on after an acute attack in which the enlargement of the gall bladder persists leads to a diagnosis of an extension to the lymph glands along the common duct. In all these conditions operation is indicated. Allow me to repeat that jaundice is not a contraindication to operation but on the

contrary often is an indication for immediate operation.

Given a case in which a tumor is plainly felt in the neighborhood of the gall bladder and in which ascites and deep jaundice are present the probable diagnosis is inoperable carcinoma, yet I have found on exploring such cases that occasionally the physical signs are caused by sclerotic changes in the head of the pancreas with lymphadenitis about the pancreas and along the common duct associated with an old chronic gall-bladder disease with adhesions, the whole pathological condition being due to gall-bladder infection. Such cases should not be denied the chances afforded for their greater comfort by operation, they should have the benefit of an exploration.

Occasionally carcinoma is diagnosed in cases of common duct stone causing intermittent jaundice and finally deep jaundice with cachexia. Such cases should also have the benefit of exploratory operation.

What has been the end result of cases so treated is shown in the following simple table which, leaving out the choledochostomies, cholecystogastrostomies and choledochoplasties, shows the end-results in 979 cholecystectomies and cholecystostomies one year or more postoperative. Those patients relieved of all symptoms are called well; those who have an occasional mild indigestion or suffer mildly from over eating and are immediately relieved by diet are classed as having mild symptoms; while those whose disabled liver, disabled from the long continuance of the infection before submitting to operation, require considerable care in diet, are classed as having severe symptoms.

Here again is plenty of food for thought. The results are fair but how much better they would have been had the patients been operated on before the liver was damaged so extensively as to require treatment even after the infecting focus was removed, and before the inflammation had resulted in adhesions, stricture of ducts, perforation, gangrene, peritonitis, cholangitis, liver insufficiency, hepatitis, liver abscess; distant infections from the local focus such as myocarditis, renal insufficiency, pulmonary infections, joint complications; involvement of neighboring organs through extension of the inflammation such as pancreatitis, perforation into the stomach, duodenum or colon, adenitis causing pressure on the common duct either beneath the liver or at or near the ampulla of Vater; carcinoma of the gall bladder following long-continued chronic irritation.

Table II

Total number of cases..... 979
Cholecystostomy..... 165
Cholecystectomy..... 814

	Cases	Per Cent
Cholecystostomy		
Well	96	58.1
Showing mild symptoms	24	14.5
Showing severe symptoms	45	27.3
Total showing symptoms	69	41.8
Cholecystectomy		
Well	705	86.6
Showing mild symptoms	79	9.7
Showing severe symptoms	30	3.7
Total showing symptoms	109	13.4
Total Cases of Cholecystostomy and Cholecystectomy		
Well	801	81.8
Showing mild symptoms	103	10.5
Showing severe symptoms	75	7.7
Showing symptoms	178	18.2

CONCLUSIONS

If the disease is considered as a focal infection the indications for the removal of such a source of infection are the same as for removal of an infected focus elsewhere, i.e., infected teeth, tonsils, appendix, etc.

While it may still be debatable, on account of the multitude of operators and the inability to check up on individual and institutional statistics, whether all diseased gall bladders should be removed, there can be but one answer as to the treatment of a gall bladder which causes continuous, repeated or disabling symptoms and that answer is cholecystectomy at a time when that operation and an exploration of the ducts can be safely done.

THE X-RAY GALL BLADDER

A SURGICAL OPINION*

V. G. BURDEN, M.D.

PHILADELPHIA

CHOLECYSTOGRAPHY is an accepted diagnostic procedure. When this method is used and interpreted by an expert and a diagnosis based on the *x*-ray findings indicates disease of the gall bladder, the diagnosis will be proved correct at operation in over 90 per cent of cases. However, in cases in which the *x*-ray diagnosis is a normally functioning gall bladder and, by inference not diseased, the percentage of error, about 26 per cent, is so great that clinical methods based on a careful history and physical examination are much more reliable. In this connection it is well to remember that the diagnosis of disease of the gall bladder on any basis shows a high percentage of accuracy because nearly every gall bladder removed shows pathologic changes. Indeed, few individuals over thirty years of age can boast of a normal gall bladder.

It is accepted by roentgenologists that absence of the gall-bladder shadow and "stone positive" are the cardinal signs of cholecystographic diagnosis. A visualized gall bladder which empties after physiologic stimulation in a specified time is regarded as having normal function. Unfortunately the latter diagnosis is often interpreted, and usually against the advice of the roentgenologist, to indicate or infer that the gall bladder is not diseased. The significance of the visualized gall bladder is a controversial subject. Perhaps the roentgenologist exceeds his limitations when he uses the term "a normally functioning gall bladder."

The proper evaluation of cholecystography should be based on an understanding of the physiology of the gall bladder and biliary tract and the changes therein incident to disease.

The two best known functions of the gall bladder are concentration and the muscular expulsion of its contents. The area of the mucosa is enormous in comparison with the size of the viscus so that one is not surprised to find that the quantity of bile entering the gall bladder becomes concentrated to one-tenth of its volume by the absorption of water. The dye, entering the gall bladder with the bile, likewise becomes concentrated, a fact which accounts for the shadow on the film. One of the inferences usually drawn when the gall-bladder shadow is absent, is that the concentrating power is impaired or lost and therefore the gall bladder must be diseased. The facts obtained from a study of diseased gall bladders do not support or warrant this assumption. Cholecystitis with or without stones usually does not impair the absorbtive function of the mucosa. On the contrary the mucosal folds are often hypertrophied and more numerous. This fact corresponds with the finding that the bile in the diseased gall bladder is usually much more concentrated than under normal conditions and is often very thick and tarry. One is safe in saying that the diseased gall bladder, except under certain specific conditions, has suffered little, if any, impairment of its ability to concentrate bile. Therefore, it is evident that the cholecystogram cannot give any reliable information regarding the concentrating power of the gall bladder. In other words, the "invisible gall bladder" cannot be explained on this basis.

* Read before the Philadelphia Roentgen Ray Society, December 8, 1932.

The mechanism by which the gall bladder empties, according to the weight of evidence, is by the muscular contraction of its walls. There is no doubt that more fluid leaves the gall bladder by absorption than through the cystic duct. It is a curious fact that during operations the surgeon never encounters a collapsed or empty gall bladder nor has he ever seen it contract in the process of emptying its contents. Not infrequently we encounter a normal gall bladder which is distended and tense. In such instances, by no amount of reasonable pressure can we cause it to empty, although there is no organic obstruction in the cystic duct. The valves of Heister in the cystic duct may act in a measure to cause retention of bile in the gall bladder and may play an important part in the mechanism by which the viscus empties. In a paper published a few years ago I drew attention to the frequent occurrence of muscular hypertrophy in the wall of the diseased gall bladder. The significance of this I am unable to state. It may indicate partial obstruction to the outlet or it may signify an irritable and overacting musculature secondary to local disease. It certainly seems to show that the gall bladder possesses in common with other hollow viscera a reserve expulsive force for the purpose of overcoming partial obstruction to its outlet. Viewed in this light, the faint *x*-ray shadow may be interpreted as being due not to deficient concentration but to hypermotility and quick emptying. The inflammatory process in cholecystitis rarely involves the muscularis but when it does, the emptying power is impaired, stasis of the bile occurs and under such conditions we would expect to find deep concentration of bile.

According to the opinions of roentgenologists, obstruction of the cystic duct is one of the important explanations of an absent gall-bladder shadow. No one will deny this simple explanation when obstruction of the cystic duct exists. However, in the total number of diseased gall bladders, complete obstruction of the cystic duct will be found in only a comparatively few cases. The diseased gall bladder usually contains bile.

Since the positive diagnosis of disease of the gall bladder by cholecystography is accurate in over 90 per cent of cases; and since the explanations ordinarily advanced for the abnormal cholecystographic findings are not supported by the pathological data it would seem that the diagnostic accuracy of the test is a paradox.

One important factor has so far escaped attention. It explains the success and failure of cholecystography. That factor is the mechanism of filling of the gall bladder. Unless bile and therefore the dye can enter the gall bladder in sufficient amount and remain there long enough for concentration, a shadow will not be cast on the film. A short review of the normal and abnormal physiology of the biliary tract will explain this point. Bile is excreted continuously by the liver, stored and concentrated in the gall bladder and discharged into the duodenum during digestion. The expulsion of digestive bile is due principally to the contractile force of the gall bladder. This contractile force easily overcomes the resistance of the sphincter of Oddi and the theory of contrary innervation has little to do with the practical working of the mechanism. But without the mechanism of the sphincter of Oddi, it is impossible for the gall bladder to fill. Regarding the anatomic and physiologic status of the sphincter of Oddi, Giordano and Mann state: "There is definite evidence of the presence of a sphincteric mechanism at the duodenal end of the common bile duct. That this mechanism represents a true sphincter and is not simply due to variations of tone of the duodenal wall has not been definitely determined, although the former would appear to be true. The discharge of bile into the intestine is modified by and in some respects depends on peristalsis of the duodenum, but the exact relationship of the two processes is not clear. Certain specimens examined at necropsy suggest the possibility that the

sphincteric mechanism can be thrown into spasm by pathologic conditions in the gastrointestinal tract and adjacent organs." The bile when it leaves the liver under excretory pressure fills the extrahepatic ducts because of the tonic closure of the sphincter of Oddi and does not enter the duodenum. Its only escape is into the gall bladder. Therefore the filling of the gall bladder is caused by the excretory pressure of the liver assisted by a closed sphincter of Oddi. There can be no other plausible explanation.

The corollary of this physiologic fact is that the gall bladder cannot fill when the sphincter of Oddi is incompetent. Certain species of animals do not have a gall bladder although they possess a sphincteric mechanism at the lower end of the common duct. However, the sphincter does not seem to function appreciably and is able to withstand only a minimum pressure which is much less than in animals having a gall bladder. The sphincteric mechanism at the lower end of the common duct bears an important relationship to disease of the biliary tract. Here is an attractive field for experimental study. At present we are concerned with its bearing on cholecystography. The question arises, how is the sphincter affected by disease of the gall bladder? Experimental study has established the fact that after the removal of the gall bladder the common duct dilates because of biliary pressure and then the sphincter of Oddi becomes permanently incompetent so that bile flows continuously into the duodenum. A similar condition develops when the gall bladder becomes functionless through disease. The observing surgeon notes the great frequency of a dilated common duct in association with a well-established chronic cholecystitis. It is impossible to state the frequency of an incompetent sphincter of Oddi in cases of cholecystitis but its occurrence is very common. Certainly it is the most plausible explanation for absence of the cholecystographic shadow except in such conditions as complete destruction of the gall bladder, empyema, complete obstruction of the cystic duct, etc. Spasm of the sphincter of Oddi is not uncommon in cases of chronic cholecystitis especially when there is associated disease of the head of the pancreas. This condition has been recognized by some surgeons who make it a practice to supplement choledochostomy by instrumental dilation of the sphincter of Oddi. It is readily apparent that spasm of the sphincter in cases of cholecystitis will insure filling of the gall bladder where the bile and the dye will be concentrated and a shadow cast although the gall bladder is diseased. Such is the explanation of the errors of cholecystography.

Both conditions of the sphincter of Oddi, incompetency and spasm, are not rare or imaginary phenomena, but are supported by reliable experimental and clinical evidence. They are also in accord with the normal and abnormal physiology of the biliary tract.

SUMMARY

1. An attempt is made to correlate the findings of cholecystography with disease of the gall bladder on the basis of the normal and abnormal physiology of the biliary tract.

2. The invisible or faint shadow of the gall bladder after administration of the dye is not caused by failure of concentration but is indicative of deficient filling of the gall bladder.

3. Without a competent sphincter of Oddi the gall bladder cannot fill. In many cases of a well-established cholecystitis, the sphincter is incompetent and therefore there can be no shadow of the gall bladder.

4. Disease and absence of the gall bladder are the only known conditions which cause incompetency of the sphincter. Hence the high percentage of *x*-ray accuracy when the report is positive for disease of the gall bladder.

5. Spasm of the sphincter in early cholecystitis is probably as common as incompetency in the later stages. In the

presence of spasm, filling of the gall bladder is insured and since its concentrating power is not impaired, a shadow will appear on the film although the gall bladder is diseased. This fact is in accord with the high percentage of error when the cholecystogram indicates a normally functioning gall bladder. It would also indicate that the cholecystogram is not a reliable diagnostic aid in early or mild cholecystitis.

6. Persistence of the *x*-ray shadow after a fat meal indicates delayed emptying and is probably accounted for by gross fibrotic deformity of the gall bladder so that it cannot completely contract and empty its contents. In some cases it may be caused by a weak and degenerated gall bladder musculature.

7. Obstruction of the cystic duct by stone, stricture or adema, obviously is responsible for an "invisible" gall bladder but this condition on the basis of pathological data is relatively infrequent and does not explain the routine positive findings of cholecystography.

8. Incompetency of the sphincter of Oddi is the most common cause of the "invisible" gall bladder.

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CARCINOMA OF THE COLON*

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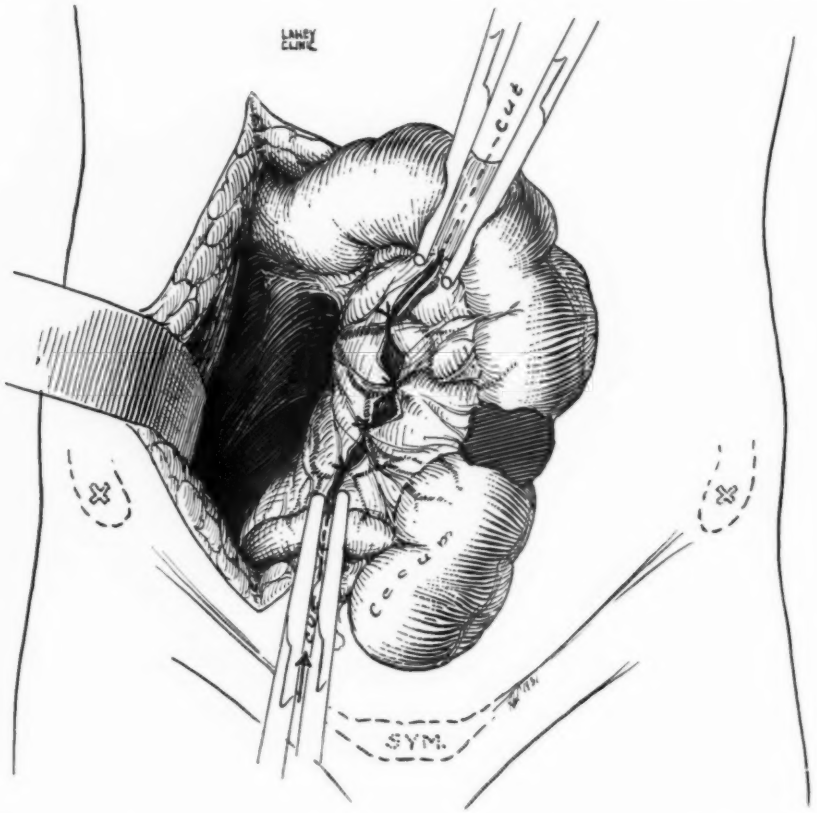
CANCER of the colon and rectum is a condition which should be frequently discussed before medical



FIGS. 1–6. Right colectomy by two-stage plan with extraperitoneal anastomosis of ileum and transverse colon after plan of Mikulicz.

FIG. 1. Mobilized ascending colon with its mesentery cut and its vessels ligated and two clamps on ileum and transverse colon between which bowel is to be severed and sterilized with cautery.

bodies. It is also a condition which should be discussed frequently before the non-medical public, because while its early symptoms are by no means tangible and striking, they are none the less real and provide warnings for further investigations; also because in our series, 56 per cent of the patients had noticed symptoms for six months or less, while 85 per cent had had abnormal symptoms for less than a year.

These lesions are, as a rule, readily demonstrable by *x*-rays and fluoroscopy with bismuth enemas, and methods of surgical removal have now been so developed and refined that they are quite safe. In addition, the anatomical location and relations of these lesions so lend themselves to wide and extensive surgical removals that the probability of cure in these cases, particularly when obtained early, is quite considerable.

The distribution of the lesion in a series in our Clinic of 153 consecutive car-

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cinomata of the colon and rectum was as follows (One patient had a lesion at the rectum, inoperable, and also at the splenic flexure, so is counted three times):

Table I
DISTRIBUTION OF LESION

	Cases	Per Cent
Cecum	14	9.03
Ascending colon	5	3.2
Hepatic flexure	5	3.2
Transverse colon	6	3.8
Splenic flexure	4	2.5
Descending colon	8	5.1
Sigmoid	21	13.5
Rectum and rectosigmoid	91	58.7
Double lesion: splenic flexure and rectum	1	0.64

Table II
AGE INCIDENCE

No. of Cases	*Years*
1	24
1	26
6	30–39
26	40–49
53	50–59
52	60–69
13	70–79
1	over 80

Of 91 cases (58.7 per cent of total), of carcinoma of the rectum and rectosigmoid, 62 per cent were in men, 38 per cent in women. Of the total of 152 cases, 48.6 per cent were in women, 51.4 per cent men.

SYMPTOMS

Table III
CARCINOMA OF RECTUM AND RECTOSIGMOID SYMPTOMS
(BASED ON 36 CASES)

At levels other than the rectum and rectosigmoid the numbers were too small for statistics.

	Per Cent
Disturbance of bowel function	88
Palpable mass	86
Lesions shown by proctoscopy	88
Definite weight loss	85
Blood and mucus in stools	83

The symptoms of cancer of the large intestine divide themselves into those symptoms of the three levels at which they occur: the proximal colon, the distal colon and the rectum. Symptoms associated with lesions arising in any one of these levels are in a considerable measure influenced by the function of the bowel at these levels.

Carcinomata of the proximal colon in, for example, the cecum, ascending colon, hepatic flexure or proximal portion of the transverse colon, are characterized by their ability to produce severe secondary anemia. So characteristic is this anemia associated with malignant lesions of the ascending colon that every case of severe unexplained anemia should be investigated for a possible undiscovered carcinoma of the ascending colon as the cause of it.

The proximal colon possesses several features which influence the symptomatology and also the results of surgery done on lesions at this level. Its lymphatic supply is richer than that of the distal colon. Its contents are of a liquid character. These liquid contents contain organisms of high virulence and toxins of a markedly noxious character, and in addition the function of this portion of the colon is to absorb fluids.

Alvarez has quite interestingly demonstrated that the degree of anemia in lesions at these levels is often quite definitely related to the size of the lesion.

The liquid character of the intestinal contents in the proximal colon eliminates largely in lesions at this level the symptoms of intestinal obstruction, and the earliest symptoms of carcinomata of the proximal colon are therefore of necessity those of vague and indefinite digestive disturbances. Lesions in the cecum and ascending colon also possess the helpful feature of being readily palpable.

The fact that the function of the distal colon is largely one of storage, and that its contents are largely solid in character and so unfavorable for the growth of organisms and production of toxins, and that little absorption occurs here, makes secondary anemia less severe and mechanical obstruction more common as an indication of the presence of a carcinoma of the colon at this level. The symptoms therefore of carcinoma of the distal colon are those of obstruction grading from acute and

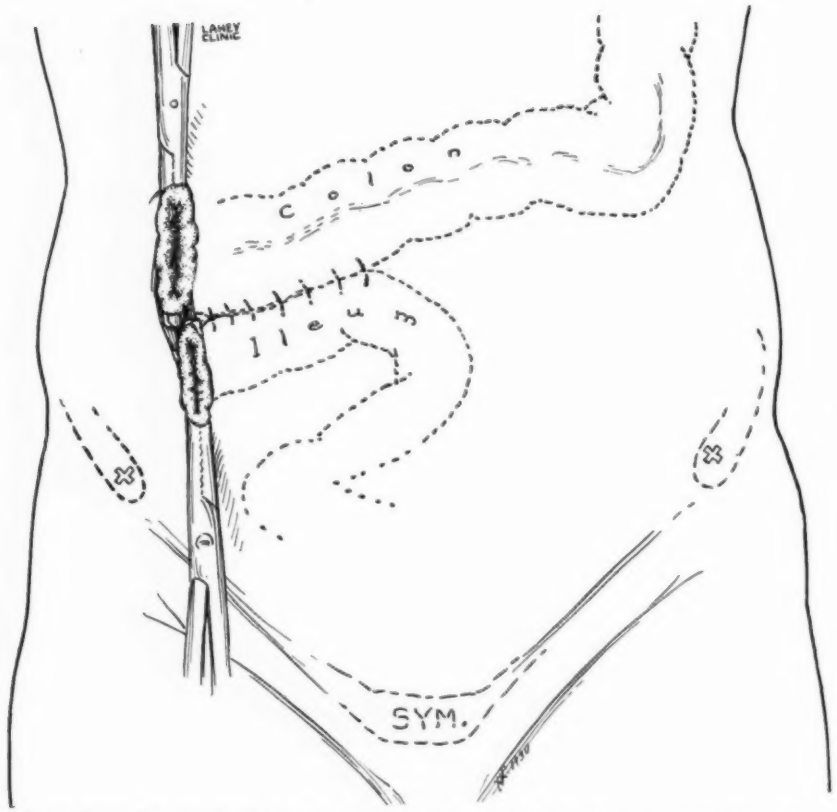


FIG. 2. Ileum has been brought up beside transverse colon, tacked to transverse colon; two clamped ends of bowel, which keep wound clean, since they do not slough off for four to six days, are implanted in wound which has been sutured about double-barrelled spur of colon and ileum.

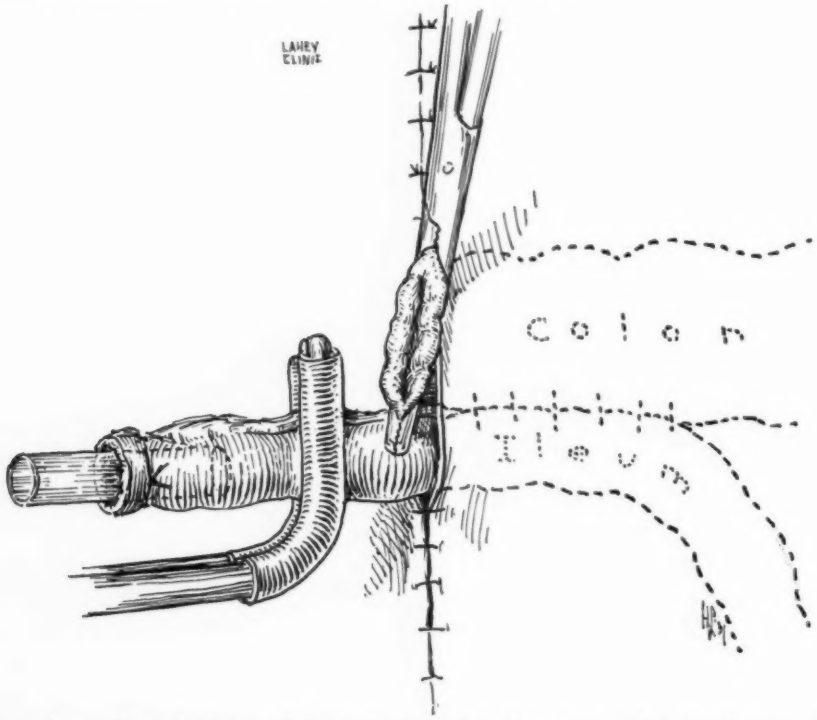


FIG. 3. Plan, where immediate drainage of ileum is desired and to be employed, of staggering ends of colon as they are implanted in wound. Note extra length of ileum pulled out into wound. In this illustration rubber-covered intestine clamp has been applied to long limb of ileum. Ochsner clamp has been removed from ileum and glass tube, which is to be connected by rubber tubing to bottle, has been tied into ileum. Protective dressing about wound during this procedure is omitted for sake of clearness and relations of two ends of bowel. At end of eight to ten days excess ileum can be cut off with cautery so that it is level with end of colon, and situation is then similar to that shown in Figure 4, except that in latter Ochsner clamps have been sloughed off.

complete obstruction down to mild and indefinite discomfort, dependent upon the varying degrees of narrowing producing only by examination solely on suspicion that early lesions may be discovered.

In a series of 100 consecutive cases of

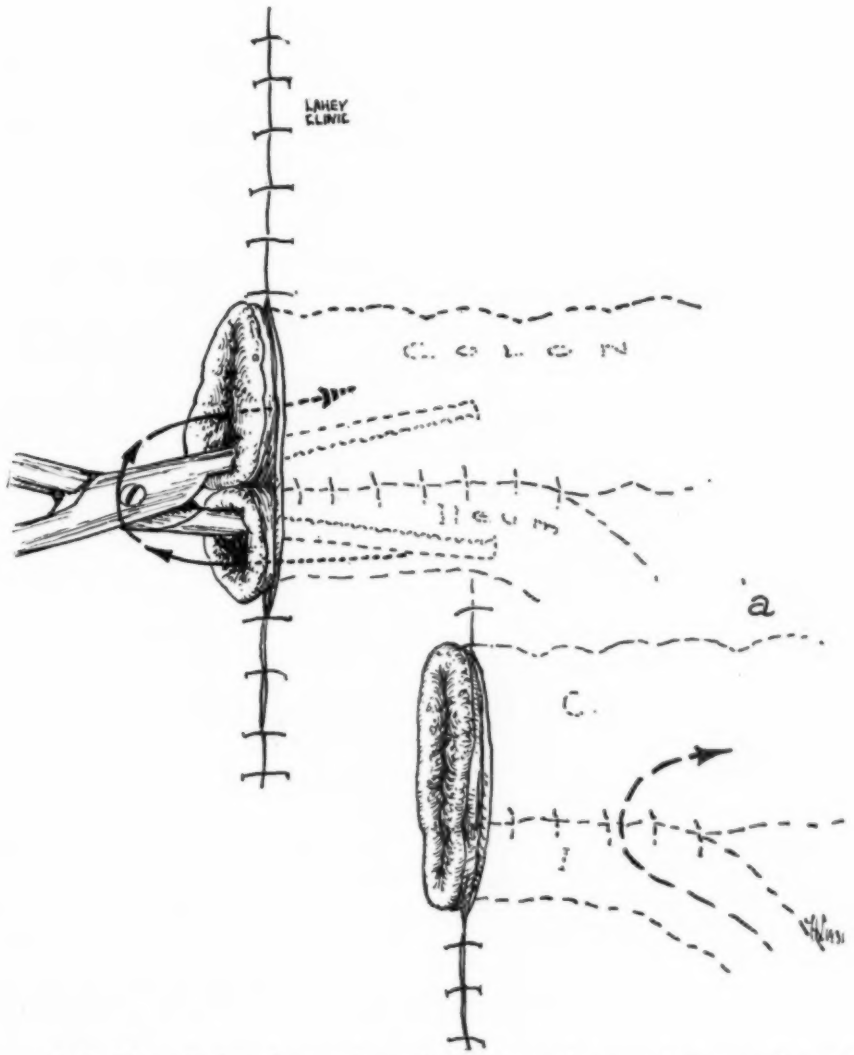


Fig. 4. Mikulicz method of introducing clamp prior to locking it so that spur between colon and ileum is caught in jaws of clamp and cut as locked clamp comes away by pressure necrosis.

Insert *a* shows external end of ileum and colon made into a common opening and arrow indicating course of feces after destruction of intervening septum.

them. Secondary anemia is rare and the lesions in the descending colon and sigmoid are often readily palpable.

Lesions of the rectum unfortunately tend to be quite silent early in their existence. The appearance of blood and the presence of hemorrhoids should obligate us to do high digital examinations and sigmoidoscopic examinations, even in the face of no symptoms whatever, since it is

carcinoma of the colon and rectum investigated in our Clinic by Dr. S. M. Jordan, as to symptomatology, some interesting information was obtained. Diarrhea and constipation occur more frequently than any other symptoms, since disturbance of colonic function must of necessity be more common than any other symptoms. In this series, constipation occurred in 56 per cent of the patients who had carcinoma

of the cecum and rectum, and in 65 per cent of the patients having carcinoma of the sigmoid. There was no disturbance in

Nausea and vomiting occur chiefly in those cases with obstruction and were present in this series in but 13 per cent of

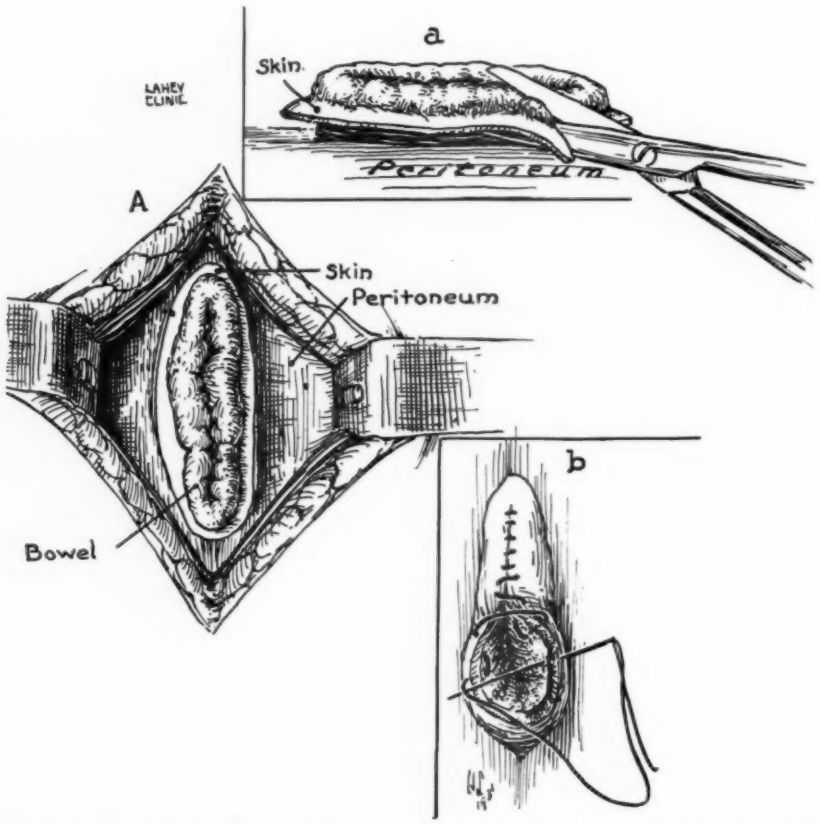


FIG. 5. Method of extraperitoneal closure of temporary enterostomy (common ileum and colon opening).

A. Skin, subcutaneous fat, fascia and muscle have been dissected away from tube of ileum and colon. Narrow strip of skin has been left attached to edge of bowel to avoid oozing from cut end of bowel. Peritoneum is still unopened and adherent to neck of protruding tube of bowel.

a. Edges of open end of bowel are being refreshed and section of adherent skin removed.

b. Open end of bowel, its vessels having been ligated, is being inverted and closed by a continuous Connell stitch of catgut and will be reinforced by another layer over this one. Note that this closure is entirely extraperitoneal as peritoneum attached to base of tube of bowel is unopened.

bowel function in only 9 per cent of the 100 cases. These data are quite convincing that there are features in the clinical history of almost all patients with this lesion which should arouse our suspicion and cause us to advise investigation. Twenty-seven per cent complained of diarrhea, half of these having carcinoma of the rectum. The textbook feature, alternating diarrhea and constipation, which is supposed to be typical of carcinoma of the colon, was present in only 8 per cent of the cases.

Weight loss was present in 65 per cent of our cases. This feature in itself is a criticism of the lateness with which the diagnosis is usually made.

Secondary anemia is by no means as frequently associated with carcinoma of the colon as would be expected. In a series of 33 consecutive cases investigated for that particular symptom, only 5 showed red blood cell counts below 4,000,000, and only 7 showed hemoglobin below 70 per cent.

A palpable tumor was found in 10 per cent of our cases. In all of our cases where the tumor was palpable, it was in the cecum or sigmoid. It is much more difficult to palpate a growth in the hepatic or splenic flexure than in the cecum or descending colon, because of the overhanging costal margins and the deep location of the colon here.

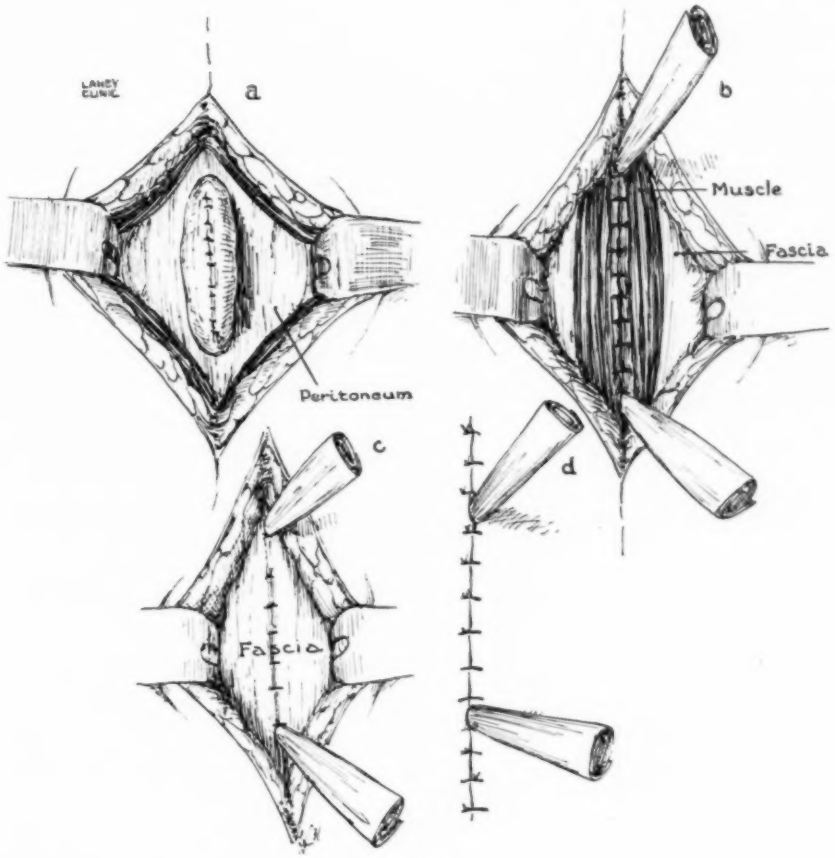


Fig. 6.

a. Enterostomy opening closed and peritoneum unopened.

b. Rubber dam drains placed at upper and lower ends of wound down to sutured bowel and muscle sutured over these.

c. Fascia closed.

d. Skin closed and drains emerging from upper and lower portion of wound.

DIAGNOSIS

The diagnosis of carcinoma of the colon would, in spite of all significant signs and symptoms, still be a matter of considerable uncertainty were it not for the invaluable aid of the *x*-ray, and our hope for increasing the percentage of early diagnoses in these lesions lies in the more frequent employment of bismuth enemas and fluoroscopy in patients showing any suggestive change in colonic function.

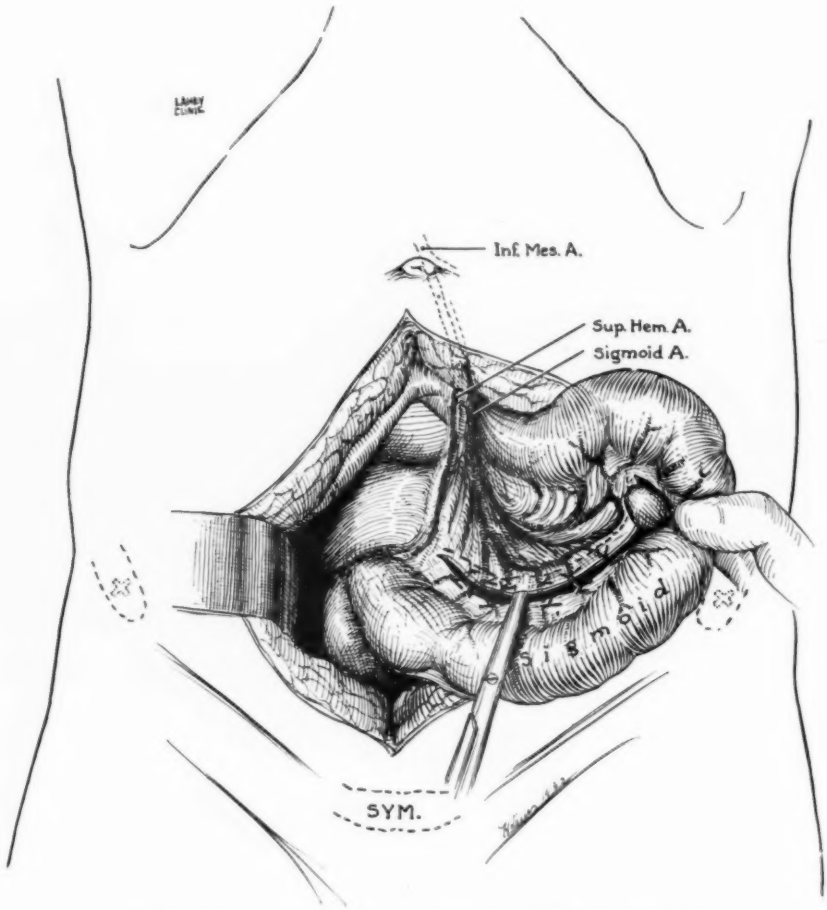
It is unnecessary for me to warn you of the need of fluoroscopy of the colon, first by means of bismuth enema, in order that an obstructive lesion may thus be demonstrated without the danger of having the barium held above the point of obstruction and producing an acute obstruction, as might happen if a barium meal were ingested.

We have had several patients with intestinal neoplasms sent to the Clinic in stages of acute obstruction as the result of taking bismuth by mouth, thus convert-

ing a patient at once from a good surgical risk into a poor one, and seriously complicating the technical management of the case.

The diagnosis of rectal carcinoma needs usually only the palpating finger for its demonstration, but in lesions of the upper rectum where the barium enema is frequently suggestive but not definite, proctoscopy and sigmoidoscopy are invaluable. The presence of hemorrhoids should not be accepted as sufficient explanation of rectal bleeding, and all patients past thirty-five years of age with hemorrhoids should be suspected of having a lesion in their rectum and should be investigated by bismuth enema and proctoscopy to rule out this possibility. Patients often resist the time, the expense and the inconvenience of bismuth enemas and proctoscopies, but when it is explained to them that the purpose of these examinations is to make sure that they do not have a malignancy higher up, their objections usually disappear.

The salvation of patients with carcinoma of the colon and rectum is in early diagnosis. Early diagnosis is undeniably dependent upon early investigations with bismuth enemas, and patients very frequently avoid gastrointestinal *x*-ray studies because of fear of their cost. We shall not increase the early diagnosis of these lesions until we have reduced the costs, particularly of bismuth enemas, so that they can be employed unhesitatingly with many nega-



FIGS. 7–11. Two-stage resection of cancer of rectum.

FIG. 7. Median incision from umbilicus to pubis, sigmoid pulled out on left abdominal wall, mesentery of sigmoid incised and its vessels ligated from mesenteric border down to but not including superior hemorrhoidal artery.

tive findings where there is only a suspicion of the presence of a malignant lesion of the large bowel.

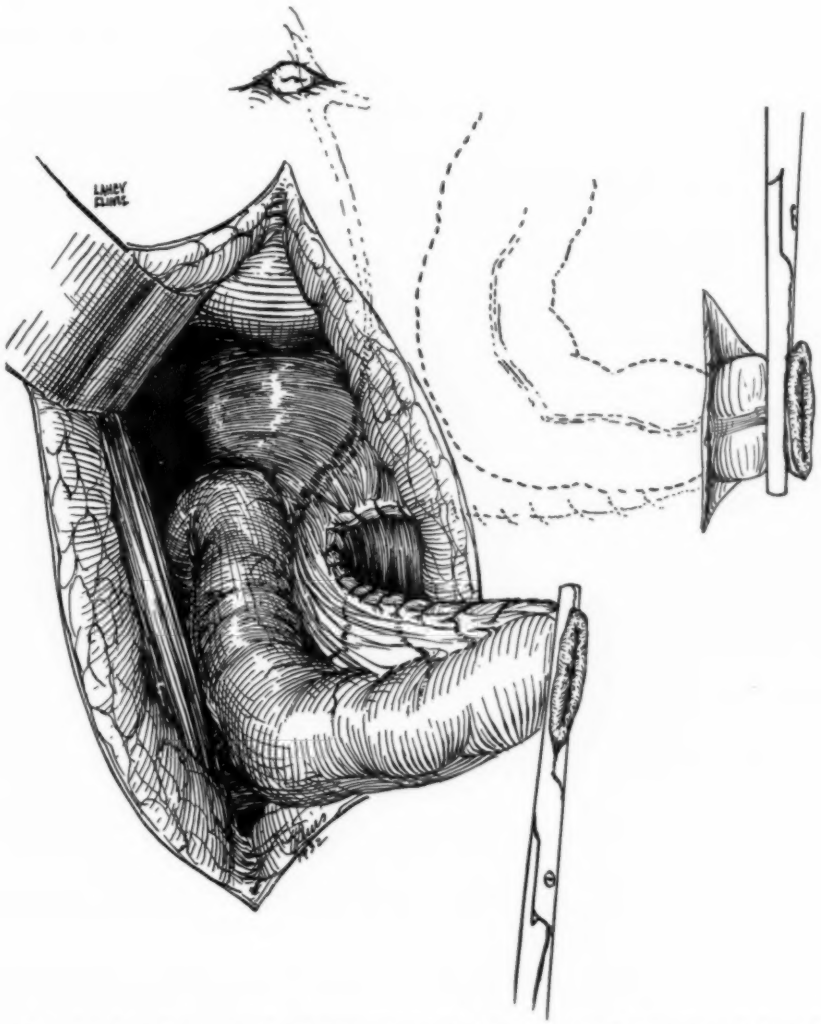


Fig. 8. Two leaves of parietal peritoneum of cut mesentery of sigmoid have been sutured, bowel has been caught between clamps and severed with cautery, its ends being sterilized. Proximal loop is pulled through left counter incision which is to be preliminary colostomy and distal loop is shown where it will be implanted above pubis. Note shadow at root of mesentery of unligated superior hemorrhoidal artery which nourishes lower segment. This permits lower segment to live indefinitely.

SURGERY

The surgery of cancer of the colon and rectum has been up to the last few years (at least in our hands) of a very serious type. Many patients coming with varying stages of obstruction have required preliminary enterostomies. Intestinal suture, particularly of the large intestine because of its sacculated character and fat tabs, lends itself quite unfavorably to safe stitch lines and anastomosis. This situation is made further unfavorable by the liquid contents of the proximal colon, rich in organisms of such high virulence, resulting so readily in the production of peritonitis by soiling on the slightest technical error or leakage. In the distal colon likewise, the security of suture lines in resections and anastomoses are often seriously jeopardized by the solid character of the feces in this segment of the colon. The presence of solid feces in this segment of the colon tends to put undue strain upon the suture line and at times to produce acute obstruc-

tion by actual blockage at the site of suture.

While this Society of Gastro-enterologists is concerned largely with the diagnosis and non-operative management of intestinal lesions, it cannot fail to be interested in the safety measures which we have developed in our Clinic to lessen the mortality of resections of malignancy of the large bowel and rectum. Illustrations, therefore, presenting the two-stage removal of the right colon, hepatic flexure and part of the transverse colon with anastomosis of the ileum to the transverse colon by the Mikulicz procedure are here submitted, with legends describing the principles of the plan and the reasons why these procedures largely eliminate the danger of peritonitis and increase the safety of extensive removals of segments of either side of the colon. Illustrations are also submitted showing the Mikulicz plan of removal of the descending colon or splenic flexure together with the staggering plan which I suggested, which makes possible the immediate drainage of the upper segment of resected bowel and the immediate relief of intestinal obstruction, a factor which distinctly decreases the degree of risk in these cases. Finally, the two-stage

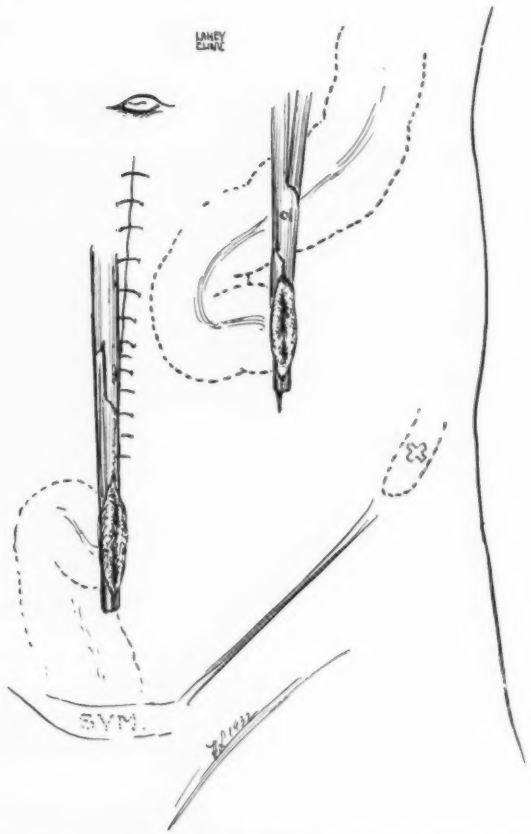


Fig. 9. Median wound has been closed about lower segment still grasped in clamp and upper segment is implanted in left colostomy still grasped in clamp. These clamps will keep the bowel grasped for four to six days by which time wound is sufficiently healed so that contamination will not occur. At end of week an anal speculum may be placed through anus and with irrigating nozzle in upper segment implanted above pubis, segregated rectum with its contained carcinoma may be irrigated through and through until it is entirely cleared of feces.

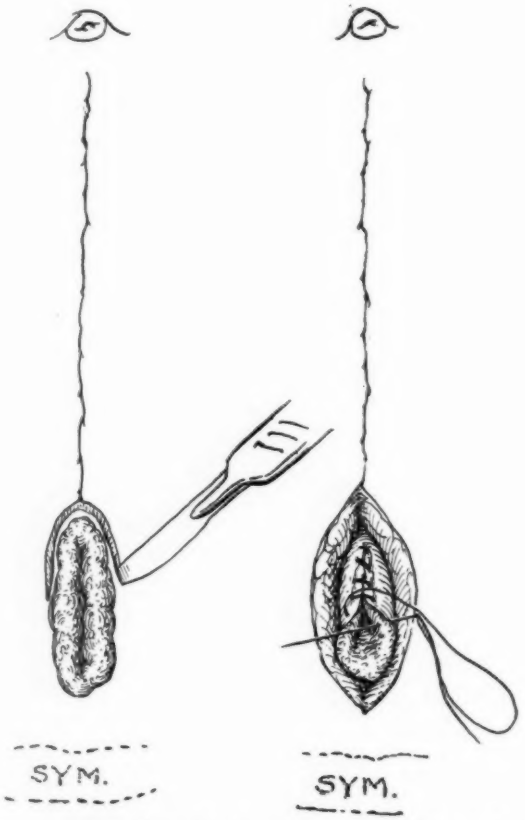


Fig. 10. Distal loop implanted above pubis ready for second-stage operation. At this stage colostomy is working well, lower segment has been irrigated thoroughly clean and has been segregated from intestinal tract and fecal contamination for two weeks or more. As shown in this Figure, at second stage an incision is made about distal segregated end of rectum or sigmoid. It is closed off, wound painted with iodine, fresh instruments taken and abdomen reopened.

plan of removal of cancer of the rectum is illustrated whereby a preliminary colostomy is established and at the same time the intention healing of the sacral wound occurs in these cases, and there is a definitely diminished risk of infection and

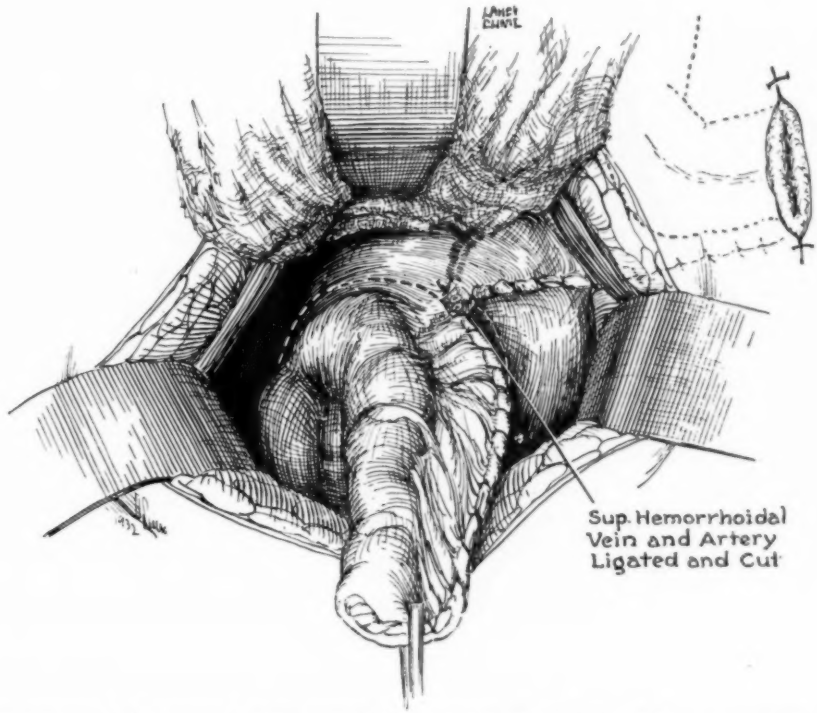


Fig. 11. Abdomen reopened for second-stage complete removal of segregated lower segment and its contained carcinoma. This is done only after bowel has been thoroughly cleaned and in presence of colostomy well established. Colostomy is covered with cocoon to prevent soiling. Note that practically only vessel requiring ligation is superior hemorrhoidal artery shown ligated at root of mesentery. Note dotted lines along parietal peritoneum incised. Segregated rectum and its contained carcinoma are pushed down into hollow of sacrum, peritoneum closed above it, abdomen closed and rectum removed from behind.
We have now performed 22 consecutive operations of this type with but one fatality and that due to pulmonary embolus.

bowel severed above the growth, implanted above the pubis and the lower segment of sigmoid and rectum containing the carcinoma so segregated that it can be thoroughly irrigated and cleansed for a period of two weeks, making it possible thus to remove a clean segment of bowel containing the growth at the second stage on a patient with a well-established colostomy and so no intestinal obstruction. First also shock.

We have been disturbed by the dangers of large intestine surgery, and we have therefore been interested during the past few years in developing these additional safety measures which largely overcome the dangers of leakage, peritonitis and obstruction so often associated with immediate removal and primary anastomoses under the older operative plans.

UNUSUAL CONDITION SIMULATING ACUTE APPENDICITIS—VINCENT'S ANGINA

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TO the long list of diseases which may be mistakenly diagnosed as acute appendicitis* must be added one which is seldom thought of in terms of gastrointestinal disturbance: Vincent's angina.

This is a comparatively recent affection, having been described by Rauchfuss in 1893, by Plaut in 1894, and by Vincent in 1896. It is characterized by the formation of ulcero-membranous lesions appearing on the oral mucous membranes. With these lesions are always associated a type of fusiform bacillus and a spirochete, and the two germs are eradicated by the same treatment. These bacilli have been found in apparently healthy mouths, but Bloodgood states that he has never seen the disease in a mouth from which all the teeth had been extracted, and from this he concludes that the germ grows in the crevices between the teeth.

Diagnosis of the disease is readily made by swabs taken from the infected areas. The Vincent's bacillus is a slender rod usually with pointed ends, often slightly bent, or even occurring in an S form. It varies from 6 to 12 microns in length. The spiral forms of the organism are long and may present from 5 to 8 curves. They are actively motile.

If the disease is acute or the inflammation has become deeply seated, there may be some fever, and the submaxillary glands or other neck glands may become swollen. The breath is always fetid, there is an increase in the salivation, and often a metallic taste in the mouth; there may be patches of pseudomembrane.

Predisposing conditions are neglected mouths, carious teeth, inflamed gums and syphilis. Cigarette smoking also has been said to be a predisposing factor.

The disease is highly contagious. During the World War whole groups of soldiers were attacked by it, chiefly those most closely confined in the trenches; hence the name "trench mouth" is sometimes used for the disease. Since Vincent's angina may be not only subacute, but chronic, there are many innocent carriers. Through chronically infected soldiers returning from the War the disease became much more prevalent in this country.

Vincent's angina is easily curable. An effective treatment is sodium perborate in about a 2 per cent solution, used as a mouthwash. Arsphenamine or neoarsphenamine solutions have been used locally and also intravenously in obstinate cases. Methylthionine chloride applied locally has also proved rapidly healing.

While the infection is usually confined to the mouth and throat, many systemic disturbances have been attributed to it. Cases of brain tumor, fatal streptococcus infection, and gangrene in various parts of the body have been recorded.

Morris reports a case in which the infection invaded the entire alimentary canal and resulted in death, as follows:

> The patient was a man of fifty, who came for treatment in April, 1927. He had been in good health all his life until about four months previous, when he developed a pain in his side and back and was obliged to give up his work as a tire builder. His physician diagnosed the trouble as neuritis. The patient kept losing weight and the pain continued. About March 1 he developed an abscessed tooth. After this was extracted his mouth remained sore, an abscess formed on his hand, he lost appetite, grew

* See Note, p. 77.

weak, and suffered pain in the right lower quadrant of the abdomen.

He was sent to the hospital for laboratory examination. A smear from the mouth was positive for Bacillus fusiformis. The blood Wassermann reaction negative. The blood count was not given. He complained of a pain in the rectum, which caused a tentative diagnosis of hemorrhoids, but he refused to be operated upon for this.

After leaving the hospital, the patient came to Dr. Morris, and examination revealed a case of gingivitis with accompanying symptoms of soreness and tenderness over the entire abdomen. He complained of extreme weakness and loss of appetite. The rectum was very tender and painful, but otherwise there was no induration, and no masses or other conditions were found to account for the pain. The blood count showed 4,200,000 red cells and 8000 white; temperature 101°F., pulse 90 to 95.

No definite diagnosis was made. The mouth improved under dental care, but the temperature and pulse began to rise and the abdomen became very tender. The patient continued to lose ground and went on to a fatal termination after two weeks' treatment.

Autopsy three hours after death showed the entire alimentary canal to be infected with Vincent's infection. The mucous membrane of the stomach was covered with small pinkish patches. The intestines had fewer patches than any other part of the tract. The appendix was normal. The cecum, descending colon and rectum were full of small patches, the rectum being very much inflamed, with some sloughing of the tissue beneath the mucous membrane. Other organs of the body were normal. The cause of death was given as Vincent's angina.

In this case while the infection had permeated the whole alimentary canal, the symptoms did not give rise to a definite diagnosis of the gastrointestinal condition. In the case that came into the writer's hands, however, the symptoms were so well defined and pointed so unmistakably to acute appendicitis that appendectomy was done.

The patient was a well-nourished woman twenty years old appearing acutely ill, with moderate fetor of breath. She came to the hospital on March 10, 1932, suffering from cramp-like pains in the lower abdomen, which had persisted for twelve hours. Her illness began with generalized pains over the abdomen, with slight nausea but no vomiting. About four hours after the onset the pain became intensified in the right lower quadrant, although the generalized pain remained. The patient had taken a purgative about three hours before admission which made her feel worse. Movements of the legs and thighs slightly increased the pain, but drawing up the thighs made her more comfortable.

The patient gave no history of previous illness. Menstruation was normal. Physical examination showed respiration of the abdominal type, marked tenderness in both lower quadrants, but more pronounced on the right side. There was a rebound tenderness. There was no definite rigidity, but the patient held herself tense when the abdomen was palpated. There was nothing else of interest in the physical examination, except a cervix very tender to manipulation, and tenderness in both fornices.

The impression was of peritonitis due either to appendicitis or to salpingitis. Because of the high temperature (103°F. on admission), absence of vomiting and exquisite tenderness on tipping of the cervix, the diagnosis of salpingitis was favored at first, and it was decided to watch the case until the next morning. The following day there was extreme rigidity of the abdomen, more pronounced in the right lower quadrant. There was some tenderness in right flank, marked tenderness on rectal examination and extreme tenderness over McBurney's point. Temperature 100°F. A diagnosis was then made of acute perforated appendicitis rather than salpingitis, and immediate operation was decided upon.

The appendix was found and the base and the mesentery ligated. The appendix was amputated with the carbolic knife—alcohol. The stump was inverted with a purse-string suture. The pelvis and upper abdomen were explored. The abdomen was closed in layers. No drains were inserted.

The uterus was found to be slightly injected, the tubes and ovaries normal. The appendix very slightly injected. There were some injection and a roughened appearance of the cecum. No free fluid was present, nor were plastic exudate or adhesions. The gall bladder

was tense, normal in color, and emptied on pressure.

Pathological report: Appendix 5 cm. long, tip not perforated. Wall 4 mm. thick. Microscopic: Moderate amount of round cell infiltration in all layers. Diagnosis: Chronic appendicitis.

On the second day after operation the patient complained of continuous pain in the abdomen. (Temperature 102°F., herpes labialis, fetid breath.) A smear was taken from the mouth for suspected Vincent's angina, which showed innumerable spirochetes and fusiform bacilli. Widal and Wassermann reactions were negative.

After the diagnosis of Vincent's angina was evident, 3 gm. of neosalvarsan were given intravenously, and immediate improvement was noticed both in the throat and abdominal symptoms, with complete subsidence of temperature.

The stitches were removed from the wound on the seventh postoperative day. A rather copious, thick, seropurulent discharge was easily expressed from the wound margins.

The following day the wound appeared to be the site of an infected hematoma arising from a stitch hole abscess. Smear and culture were taken from the discharge.

By the tenth day after operation all objective signs of Vincent's angina had cleared up in the mouth and throat, and precautions against infection were removed.

Two weeks after operation, the wound appeared to be healing well and the patient was discharged.

Unfortunately the smear from the wound became lost, so that no report of findings is possible. The culture, however, showed no growth of organisms. This would have been the case had Vincent's bacilli been present; but would not have been the case with the organisms commonly found in appendicitis.

The fact that acute infections often give rise to symptoms that may be mistaken for those of acute appendicitis, such as abdominal pain and vomiting, followed by a rise of temperature, has been noted by other observers. Royster remarks that appendectomies have been done when the real cause of the trouble was a chronic infection of the accessory sinuses of the nose, and that tonsillectomy often clears up suspicious cases of chronic appendicitis.

The fact remains, however, that when symptoms of acute appendicitis are seen in association with acute infections in other parts of the system, the chances are that appendicitis is actually present.

A marked increase in the incidence of appendicitis has been noted after epidemics of influenza and other infectious diseases.

Reuter reports a case of his own in which acute appendicitis followed closely upon an attack of Vincent's angina. He states that such a sequel to angina has frequently been noted and that in such cases the appendicitis is often particularly severe and shows a definite tendency to gangrene.

In his case, the patient was a man of twenty-two, suffering from Vincent's angina, with a large ulcer on one tonsil. The ulcer healed slowly under neosalvarsan and tryaflavin medication, but in the course of three days violent pain developed in the right lower quadrant. Appendectomy was done the next day. The appendix showed a purulent content with beginning gangrene. The original smear disclosed abundant fusiform bacilli and a few spirilla. Culture of the appendiceal content showed only a few Gram positive diplococci, but no aerobic or anaerobic microorganisms developed. No colon bacilli were observed or cultivated.

Reuter believes the germs to have reached the appendix by ingestion, rather than by way of the blood and lymph. A piece of necrotic tissue from the tonsillar lesion may have overloaded the stomach with bacteria which the hydrochloric acid was insufficient to destroy.

These 3 case histories, Morris', Reuter's and the writer's, clearly demonstrate the danger of Vincent's angina to the gastrointestinal system. It is seen greatly to complicate the diagnosis of acute appendicitis, for which, unfortunately, there is no pathognomonic sign.

In the writer's case, Murphy's syndrome was present in its entirety, with immediate

appendectomy clearly indicated, yet there was no acute appendicitis.

On the other hand, as illustrated in Reuter's case, there is no reason why Vincent's angina and acute appendicitis should not coexist, the latter usually of the gangrenous type, in which it is hazardous to delay operation.

In view of these facts, the physician who is confronted by a case of Vincent's angina accompanied by acute appendiceal symptoms must make a prompt decision whether or not to operate. An unnecessary operation may well be regarded as the lesser evil.

In any case of Vincent's infection, the writer recommends treatment by intravenous injections of arsphenamine or neoarsphenamine, rather than by local applications, in order to counteract any systemic infection that may exist. Fortunately the results of this treatment are rapid. The angina clears up quickly and unless there is a real appendiceal lesion, the abdominal symptoms rapidly follow suit. Should they persist, of course, immediate operation is in order.

NOTE

The conditions which simulate acute appendicitis, as compiled from various leading authorities, are as follows:

- Perforating peritonitis from ulcer, malignancy, etc.
- Stone colics of biliary, renal, ureteral and pancreatic duct regions
- Twisted pedicles of ovarian cysts
- Ileus from strangulation, obturation, intussusception and volvulus in the ileocecal region or of the sigmoid
- Chest conditions, such as lobar pneumonia, acute pericarditis, coronary thrombosis and dissecting aneurysm of the descending aorta
- Spinal lesions, such as tabes, myelitis and vertebral osteomyelitis
- Intra-abdominal hemorrhage from ruptured ectopic pregnancy, ruptured uterus, ruptured ovarian cyst, bleeding corpus luteum, ruptured aneurysm, abdominal conditions with bleeding from liver, spleen or mesenteric vessels
- Herpes zoster initial neuralgia
- Pyelitis
- Dietl's crisis
- Acute salpingitis
- Ectopic pregnancy (both before and after rupture)
- Acute epididymitis
- Dysmenorrhea
- Diverticulitis
- Tuberculous peritonitis
- Thrombosis and embolism of the mesenteric vessels
- Carcinoma of the cecum.

Among the more obscure or rare abdominal conditions sometimes mistaken for acute appendicitis, are:

- Intestinal obstruction by Meckel's diverticulum
- Spasm of the small intestine
- Torsion of the omentum
- Rupture of the right rectus abdominis muscle
- Acute leukemia
- Unperforated ulcers of the terminal ileum
- Contracture of the psoas parvus muscle.

Tuberculosis of the abdominal organs, typhoid fever, and mesenteric lymphadenitis produce symptoms similar to those of acute appendicitis, as do the prodromes of the acute exanthemata common in childhood.

Conditions characterized by a milder onset of symptoms are:

- Acute indigestion
- Acute gastroenteritis
- Colitis
- The pseudo-appendicitis of Nothnagel
- Cecum mobile
- Typhlatony
- Intestinal parasites, especially thread and round worms
- Membranes and adhesions of the right lower quadrant
- Chronic obstipation
- Chronic rheumatoid arthritis of the spine
- Pott's disease of the spine developing nerve root symptoms
- Neuritis and neuralgia of the ilioinguinal and iliohypogastric nerves.

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ROENTGENOLOGIC VISUALIZATION OF THE PERIPHERAL NERVES; NEUROGRAPHY IN VIVO

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NAGOYA, JAPAN

LITERATURE

DANDY was the first to apply roentgenography to the brain of a human being. He was successful in making roentgenograms by means of the injection of gas, such as air or oxygen, into the ventricles of the brain and subarachnoid space by means of lumbar or ventricle puncture; since then this method has been universally applied to clinical cases, and has been proved very useful in the diagnosis of brain tumor. It is also maintained by Dr. Saito, one of the authors, that this is one of the best methods for this procedure. It is also recommended that, instead of gas, we inject lipiodol, iodipin, campiodol and moljodin into the ventricle or subarachnoid space, by means of which we can carry on clinical encephalography and myelography. Apart from these, there were few who tried roentgenography of the peripheral nerves (neurography).

However, on an encephalogram by air injection one can perchance recognize a part of a peripheral nerve; that is to say, the chiasm of the optic nerve will be recognized among the shadows of the chiasmatic cistern, or, as shown in Figure 1, the oculomotor nerve may also be recognized in the interpeduncular cistern as a small line; and in the case of a myelogram, taken by means of the injection of iodized oil into the spinal subarachnoid space, the intraspinal part of the spinal nerves or the figure of the cauda equina will be clearly seen.

The roentgenological representations of nerves as just explained are visualized only in the intradural part, and it is unusual to record on the film the extradural part of nerves, i.e., the picture of a peripheral nerve in vivo. It was reported that when Haguenau and Gally injected at the foramen ovale with lipiodol as a therapeutic test in the case of trigeminal neuralgia, the oil was infiltrated through the maxillary nerve, and by chance the roentgenological contour was visualized. According to the report of Prof. Funaoka (Anatomical Institute of the Kyoto Imperial University, Japan) when, in a study of intraneural injections, he injected a solution of chloroform with various medicaments into the sciatic nerve of a mouse, it caused a general anesthesia; taking advantage of this general anesthesia, he injected a solution of lipiodol in chloroform into the sciatic nerve, by means of which he was successful in taking the neurogram.

The making of neurograms in vivo was carried out successfully by us by the following method, and this procedure was proved to be applicable to clinical cases:

The substance used in blood-vessel visualization by Saito, Kamikawa and Yanagizawa, was l'ombre, which, as it was reported, is an emulsion prepared with iodized oil (lipiodol, iodipin, moljodin and campiodol) mixed with recithin, honey and water.

This substance will not stimulate the endothelium at all, even if it injected into the artery, and so it will cause no pain to the patient. This substance causes a minimum of irritation even when injected into tissues. This emulsion is recommended as the ideal one for neurographic use, because it will neither give any pain even if injected intraneurally, nor cause any paralysis of the nerve after its injection.

METHODS OF INJECTION

There are two methods of injection: (1) intraneural, i.e., the endoneural injection method; (2) perineural, i.e., the interneural injection method.

(1) Intraneural (Endoneural) Injection Method. This method may be called the "surgical injection method" or the "incision method," because in this method L'ombre is injected into the nerve by means of a syringe with a thin needle, after the nerve has been exposed by a surgical operation. In this case, how much emulsion will be injected is chiefly determined by the size of the nerve; however, for even such a big nerve as the sciatic, 0.5–2 c.c. is sufficient.

The emulsion of oil injected into the nerve will clearly show in the neurogram after it infiltrates into the fibers of the nerve.

(2) Perineural or Interneural Injection Method. This method is applied to the brachial and the lumbosacral plexuses. In this method, as the emulsion of lipiodol is injected into the tissues between the nerves, the latter will remain transparent in roentgenograms against the emulsion, while the former will show clearly in the shape of black bands. On the contrary, when the intraneural injection method is employed, the shadow of the nerve will be visualized.

(*a*) *Perineural Injection Method in the Brachial Plexus:* The technique of this method is entirely the same as that of the plexus anesthesia of Kulenkamff, that is to say, the pulse of the subclavian artery is located at the upper part of the middle of the clavicle, the injection needle is put just outside of the artery, and then 20 c.c. of l'ombre are injected between the nerves coming out from the scalenic triangle on the upper part of the first rib. Thus the injected l'ombre will be allowed to infiltrate into the tissue between the nerves.

(*b*) *Perineural Injection Method in the Lumbosacral Plexus:* This method is just the same as that which Cathelin applied to sacral anesthesia. L'ombre is injected by a needle through the sacral hiatus; from 10–20 c.c. is quite sufficient.

The intraneural injection by the foregoing methods should be done quite slowly and gradually, otherwise the emulsion will overflow outside of the nerve. When the nerve has received the injection, it will naturally swell up; but, after a while, as the

Fig. 1. Op, optic nerve. P, pons cerebri.

emulsion begins to flow between the neurofibers from the point of injection to the center of the nerve, we will be able to make a fine roentgenological picture of the nerve.

By the foregoing method we have practiced neurography in the following cases:

Case I. K., female, aged sixty-nine years, fracture of right femur and right tibia.

In the process of arteriography on the right leg 1.5 c.c. of l'ombre were injected into the fibular nerve in the popliteal fossa. In this case, we discovered that the emulsion of lipiodol had infiltrated about 7 cm. up from the point of injection, namely, up to the center of the sciatic nerve, when the roentgenogram was made on the next day; two days after the injection, the film showed the infiltration of the emulsion up to 15 cm. from the point of injection, and in the roentgenogram made four days after the injection, we can observe the shadow of the emulsion in the nerve somewhat reduced in density, and the nerve fibers distinctly recorded.

Case II. N., male, aged sixty-three years, Buerger's disease of both legs.

In this patient, 1 c.c. of emulsion of lipiodol was injected into the fibular nerve during arteriography of his right leg. In the process we could visualize fine nerve fibers of the nerve 10 cm. in length along the course of the distribution of the emulsion in the sciatic nerve.

The right leg was amputated at the middle of the femur, then 1.5 c.c. of emulsion of lipiodol

were injected into the sciatic nerve. Several days later, when a roentgenogram was made, we could observe the emulsion infiltrated

Case IV. S., male, aged twenty years, complicated fracture of the right radius, ulna and humerus.

Fig. 2. Case I.

Fig. 3. Case II.

Fig. 4. Case III.

12 cm. upwards in the sciatic nerve. Again, two weeks later, in a roentgenogram, it was observed that the emulsion had infiltrated 14 cm. upwards in the nerve. At the end of seven weeks we could see roentgenographically only a slight quantity of l'ombre, almost all the emulsion having been absorbed.

Case III. O., male, aged twenty-one years, tuberculosis of right ankle joint.

One and five-tenths cubic centimeters of l'ombre were injected into the fibular nerve during arteriography on the right leg. On the next day we observed that the injected l'ombre had infiltrated 10 cm. from the point of injection toward the center of the nerve, and about 5 cm. in the peripheral direction. In the roentgenogram the nerve was visualized with the figure of fine fibers. Again, one week later, in another roentgenogram, we observed that the emulsion of lipiodol had been a little absorbed.

The right arm of this patient has been amputated at the middle of the humerus, and at the operation 0.5 c.c. of l'ombre were injected at the amputated ends of the radial, ulnar and median nerves respectively. On the next day in the roentgenogram, we recognized the infiltration of the emulsion of lipiodol 12 cm. upwards in the radial nerve, and 10 cm. upwards in the median and ulnar nerves; that is, the nerves were finely visualized roentgenographically up to the axillary nerve.

After the injection on each of the first, second, third, eighth, twelfth and thirty-third day, we studied roentgenographically the condition of the resorption of the emulsion of lipiodol injected into the nerve, and learned that it was absorbed a great deal on the twelfth day, while on the thirty-second day it was almost wholly absorbed and only a little of it could be traced.

In the 4 cases reviewed, we injected twice in the peroneal nerve, once in the sciatic nerve, once in the tibial nerve, be-

Fig. 5. Case IV. R, radial nerve. Br, median and ulnar nerves.

sides injections in the radial, ulnar and median nerves; and so, in all, 7 intraneural injections were made. The emulsion of lipiodol, l'ombre, which is used in blood vessel visualization, is injected only in the peripheral nerve to enable us to take the neurogram by means of the intraneural infiltration of the emulsion; and at this juncture, as the emulsion infiltrates between the neural fibers, the record of the neural fibers is distinctly visible in the roentgenogram.

DIRECTION OF INFILTRATION

Now as to the direction of the infiltration of the injected emulsion from the point of injection, that is to say, whether it infiltrates in the peripheral or central direction, it has been proved in all cases that it does not infiltrate very far in the peripheral direction, and consequently we can see that the contour of the peripheral part of the nerve is demonstrable only a short distance from the point of injection. On the contrary, the infiltration runs in the central direction easily, and infiltrates rapidly for a longer distance than in the peripheral direction, so we can record roentgenographically the shadow of the nerve all the way from the point of injection to the central part of it.

We can see the infiltration of the emul-

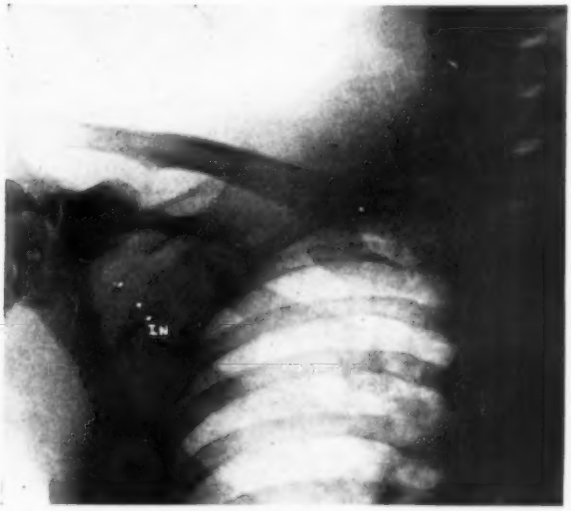

Fig. 6. Case V. IN, lipiodol solution injected in interneurol spere.

sion as far as 10 cm. within a few hours and up to twenty-four hours after the injection, and the infiltration will be extended in the central direction as far as 15 cm. if it is left for a longer time, but it will not go so far towards the peripheral part. From the foregoing facts, we know that the direction of the diffusion of the injected emulsion shows the direction of the lymph stream in the nerve, namely, that even in the nerve there runs a lymph stream, in just the same form as it is seen in the other parts of an extremity, running from the periphery toward the center, which will naturally transport the injected emulsion from the point of injection centrally. On the contrary, the injected emulsion will not run so easily in the direction opposite to the lymph stream, namely, peripherad. However, if it is injected with high pressure it will be found to flow a few centimeters from the point of injection. Thus, in the practice of neurography, it is quite essential to inject the emulsion exactly at the point of the periphery close to the nerve that is the object of the roentgenography. If the nerve is cut or suffers from neuritis, neuroma and cicatrix, the infiltration of

the emulsion will be disturbed, and something abnormal in the roentgenological appearance of the nerve will be visualized.

This procedure, therefore, can afford us a means of accurate roentgenological diagnosis in the pathological changes of a nerve. In the shadow of the normal nerve, we can clearly visualize the appearance of the fibers arranged in parallel; if the visualized structure of the fibers is disturbed, or has been cut, we can see all these conditions in the film, and by means of it we can pursue a detailed roentgenological histologic study.

RESORPTIVE PHENOMENON

(1) Resorptive Phenomenon of Emulsion of Lipiodol Injected into the Nerve. In order to observe the absorptive phenomenon of the emulsion of lipiodol injected into the nerve, many roentgenograms were made at various times after the injection, namely, from twenty-four hours up to thirty-three days. We have visualized neurograms at intervals, and observed that the shadow of the emulsion of lipiodol injected into the nerve became less and less dense from the twentieth day, and that on the thirty-third day only a slight trace of the emulsion remained. From the foregoing fact, it seems to us quite reasonable to suppose that the entire resorption of the emulsion of lipiodol injected into the nerve will require about one month.

(2) Perineural, or, Interneural Injection Method: We use this method of injection in both the brachial and the lumbosacral plexus; we are, therefore, illustrating each of these:

(a) *Clinical cases of the interneural neurography of brachial plexus:*

Case v. T., male, aged twenty-one years, genuine epilepsy.

We practiced the technique with this patient according to the brachial plexus anesthesia by Kulenkampff, and injected 5 c.c. of the emulsion of lipiodol into the plexus by means of a needle introduced at the upper edge of the clavicle.

In this case, on examination of the shadow of the nerve in the roentgenogram, we observe, in many linear markings, the aspect of the emulsion of lipiodol injected into the interneural sphere, and the shadow is displayed in its progress to the axillary fossa, passing by the outer borders of the first and second ribs: and in the arrangement of the shadow lines, we can also observe the nerve, artery and vein in the form of a hempen cord. In the roentgenogram which was made on the day after the injection, we observe the shadow of the emulsion of lipiodol diminished by the effect of the resorption: after one week the shadow was further diminished, but not entirely absorbed.

From Case v, we learn that the emulsion of lipiodol injected into the brachial plexus will be diffused after infiltrating to the periphery from the point of injection. This emulsion, as it infiltrates into the connective tissue between the nerves, and into the nerves and artery, will form a negative shadow when the artery and nerves are penetrated by the *x*-ray. If the emulsion is injected into the connective tissue between the nerves, the direction of diffusion will be quite contrary to that in the case of intraneural injection, and the resorption will be rather quicker than in the former.

(b) *Neurography of lumbosacral plexus:*

In order to make a roentgenogram of the lumbosacral plexus, as in Cathelin's method of injection, or in the same method of sacral anesthesia, epidural injection is carried out by puncture of the sacral hiatus, the volume of the injection being 5–20 c.c. This method was practiced, first of all, in a cadaver in the following case:

Case vi. Lumbosacral plexography in a cadaver: male, aged fifty-four years.

By the foregoing method, 20 c.c. of emulsion of lipiodol were gradually injected into the spinal canal of the cadaver soon after death. We observed the diffusion of the injected emulsion in three directions; the upward diffusion reached as far as the upper part of the second lumbar vertebra. The emulsion, flowing up the extradural space of the spinal canal, showed the canal and the sulcus medi-

anus of the spinal dura mater very clearly; while as the emulsion flowed downwards along the outside of the spinal cord at the point of penetrating the dura, its shadow was followed for many millimeters, and the more it ran down, the more the diffusion along the nerve increased in length. When the emulsion reached as far as the sacrum, it diffused for a considerable distance along the nerve, that is to say, the emulsion of lipiodol coming out from the anterior sacral foramina was divided towards the right and the left a little below the iliosacral articulation, and ran out along the nerve divergently, keeping an angle of 40° against the median line. In the experiment, we observed that the diffusion on the right side reached as far as 10 cm. from the median line, while the extent on the left was about 15 cm., and in the latter case, we could follow the diffusion as far as the region of the hip joint. Moreover we visualized the nerve as a shadow like a long hempen cord in the shadow of the emulsion of lipiodol diffused along the interneural connective tissue.

Lumbosacral plexography was also practiced *in vivo* in 3 cases as follows:

Case vii. W., male, aged twenty-three years, genuine epilepsy.

In this case, 10 c.c. of the emulsion of lipiodol were injected into the patient by the foregoing method, and we observed that the emulsion was diffused as far as the upper part of the third lumbar vertebra, infiltrating the left side. As for the diffusion along the lumbosacral nerve, the emulsion almost reached up to the point where the nerve came out from the anterior sacral foramen, so that we could clearly visualize the outlines of the nerve tissue.

Case viii. A., male, aged forty-three years, bronchial asthma.

In this case, 5 c.c. of the emulsion of lipiodol were injected into the extradural space through the sacral hiatus, and we observed that the injected emulsion was not diffused upwards so far as in Case vi but the diffusion reached almost up to the lumbosacral articulation, chiefly along the right and left plexuses, which come out from the first, second, and third anterior sacral foramina. On the right side, the diffusion almost reached the coxal articulation, while on the left it was not so close as it was on the right, but not far from that point; however, the shadows of the diffused emulsion were formed with small lines along the nerves, and among the lines the shadows of the nerves were clearly visualized. In this case, the emulsion was injected only through the sacral hiatus, but the injection needle was not introduced deeply into that part. Thus the plexus was clearly visualized, while the spinal cord was not.

Fig. 7. Case vi. SM, sulcus medianus. R, radix of spinal nerves. LS, lumbosacral plexus.

Case ix. M., female, aged twenty-one years, elephantiasis of the right leg.

This patient, after having had two operations on the right leg, and the skin on that part cut off, had 20 c.c. of the emulsion of lipiodol injected through the sacral hiatus. At the time of injection she felt a little swelling of the part. On the roentgenogram, we saw that the emulsion of lipiodol did not run so high up in the spinal canal: and we could observe the shadow of the lumbosacral plexus clearly by the diffusion of the emulsion as far up as 3 cm. along the nerves which come out on both sides through the anterior sacral foramina.

By these experiences, we know that the emulsion will run in the epidural space of the spinal canal up to the 2nd lumbar vertebra, if the emulsion of lipiodol is

injected into the epidural space, the injection needle being introduced through the sacral hiatus; then the emulsion will to a considerable distance, and to the same degree on both sides, as was evident in our work.

Fig. 8. Case vii.

Fig. 9. Case viii. LS, lumbosacral plexus.

diffuse along the nerve as it comes out from the spinal cord, and by this means the shadow of the nerve may be visualized. In this case, therefore, epidural or extradural myelography of the lumbar cord, as well as the roentgenography of the lumbosacral plexus, will be possible.

When the emulsion is injected not too deeply by the injection needle, as it will diffuse principally along the sacral plexus, it will run out of the front part of the anterior sacral foramen close to the gluteal nerve, then the emulsion will form a pattern of parallel lines, or of a shadow like a cord, and by this means the roentgenography of the plexus is possible. In one case, in which the injection needle penetrated partially on one side, epidural infiltration of the emulsion took place only on that side. If the volume of the injected emulsion is too great, for instance, if 20 c.c. be injected, then it will infiltrate upwards

From these experiences, we learn the process of infiltration of saline waters injected by Cathelin's method, and, at the same time, we can study the process of the diffusion of the anesthetic in sacral anesthesia; again, as roentgenography of the lumbosacral plexus and extradural or epidural myelography will be possible when the infiltration of the emulsion of lipiodol runs up so high, we believe this method will be applicable for the diagnosis of lumbar spinal tumor and of neuroma in the lumbosacral plexus.

CONCLUSION

Neurography in the foregoing experiments was successfully carried out by means of injection of the emulsion of lipiodol into the intraneural or interneural sphere, and it was ascertained that no unfavorable symptoms followed during

and after the injection, such as pain during the injection, fever, neuralgia or paralysis. By intraneural injection, the emulsion will diffuse towards the center of the part, while in the case of interneural injection, it will diffuse towards the periphery; and the resorption of the injected emulsion will soon take place. In the case of intraneural injection, the resorption of the injected emulsion will take much longer than in the case of interneural injection. By these methods, we can be successful not only in neurography, but epidural and extradural myelography will also be possible, if the emulsion is injected through the sacral hiatus. We believe that by the foregoing methods, some particular diseases of the nerves, such as neuritis, amputation of nerves, neurinoma and spinal tumor can be examined.

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*Continued from p. 134.

CORAMINE IN DENARCOTIZATION AND RESUSCITATION*

A PRELIMINARY REPORT

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DURING the past twenty-seven months, there has been the opportunity closely to observe the action of and recovery from several different anesthetic agents, used according to various techniques and with different forms of preliminary medication. In all, there were more than 1700 patients, operated upon by the same surgeon; but the present discussion is concerned only with 110 cases where avertin was used for basal anesthesia and one case where spinal anesthesia with novol was employed. In the last 82 of the avertin cases, coramine (a 25 per cent solution of pyridine-beta-carbonic acid diethylamide) was administered routinely in a dose of 2 c.c. immediately on return to bed and also according to special indications. The 28 cases of avertin basal anesthesia immediately preceding these 82, coramine-treated ones, served as controls, careful records being kept. In the patient given spinal anesthesia, coramine was administered in the presence of severe collapse.

Only 7 of the 83 patients received hypnotic medication the night before operation; these were given phenobarbital in doses of 1½ gr. One hour before operation, morphine sulphate, gr. ⅙, and atropine sulphate, gr. 1/150, were injected subcutaneously; and fifteen minutes later, 2.5 per cent solution of avertin administered rectally in from fifty to 180 seconds, except in the patient given spinal anesthesia. The dosage of avertin varied from 55 mg. per kg. to 80 mg. per kg., 5 per cent of the patients receiving the smaller amount, and 20 per cent, the larger; while the remaining 75 per cent were given approximately 72 mg. of avertin per kg., with the result that all but three were asleep when brought to the operating room forty-five minutes later. In most of the patients, nitrous oxide-ether was administered by the closed method, with absorption of the carbon dioxide by soda lime; the others, with the exception of one receiving ether by the open drop method and the one given spinal, were anesthetized by the regular nitrous oxide-oxygen or nitrous oxide-carbogen mixture, with addition of the amount of ether necessary to secure relaxation. Avertin used as a basal anesthetic in this manner not only has rendered the ordeal much less trying to the patient but has proved most convenient for hastening the onset of surgical anesthesia. Prior to the employment of avertin, much difficulty was experienced in getting the patients sufficiently relaxed in the five minutes allowed between cases.

In spite of the obvious advantages of this agent, avertin may produce undesirable effects. In the first place, although the amounts employed were well within what is considered the limit of safe dosage, 7 of the patients developed alarming symptoms of respiratory and circulatory depression, due, undoubtedly, to unusual susceptibility on their part. Abnormally high systolic blood pressure appears to bear a definite relationship to this susceptibility; instances where this pressure exceeded 165 mm. all showed a drop of 70 mm. or more. In the presence of severe respiratory and circulatory depression, one has to deal with an emergency where prompt restorative measures must be instituted.

A second disadvantage of avertin, shared by certain other general anesthetics, is the prolonged period of postoperative unconsciousness. The lowered pulmonary ventilation, depressed or absent cough reflex, and slowed circulation which are present to a

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greater or lesser extent during this period undoubtedly predispose to pulmonary complications. Of importance is the fact that special attention is necessary with these unconscious patients, demanding the constant attendance of a nurse.

Both acute collapse and unduly prolonged unconsciousness from avertin are due to exaggerated depression of the central nervous system by the anesthetic. Theoretically, this depression may be overcome by removal of the depressing agent; either by hastening detoxication in the body or elimination from it. With the demonstration by Welsch,[47] Straub,[44] Endoh,[10] and Eichholz[9] that avertin was detoxicated through conjugation with glycuronic acid, attempts were made to utilize this latter substance as an antidote for avertin; unsuccessfully, however, because conjugation depends not only on the supply of glycuronic acid but also on the metabolic activity of the liver.

Thyroxin exerts a profound influence on hepatic metabolism; this being recognized, it has been employed with the object of hastening detoxication of avertin. In the initial experiments of Lendle,[25] it was found that the duration of avertin unconsciousness could be slightly reduced in rats if the animals were previously treated with thyroxin. From clinical observations, Pribram[35] concluded that by thyroxin administration it was possible to regulate avertin unconsciousness to a certain extent, but subsequent studies have failed to confirm this. Nell and Sebening[31] find that it is necessary to administer thyroxin in amounts and over a period sufficiently great to increase the metabolic rate 30 per cent in order to affect the duration of avertin narcosis. Especially significant were the results of Stark.[43] This author observed that when thyroxin was administered in large enough doses to cause distinct evidences of hyperthyroidism, the excretion of glycuronic acid in the urine, instead of being increased, was actually diminished, and, accompanying this lowered excretion of glycuronic acid, the period of unconsciousness from a given dose of avertin was prolonged. The explanation for such a result may lie either in loss of liver glycogen from the elevated metabolism or in actual hepatic damage from excessive dosage with thyroxin. Since the effect of thyroxin is not manifest for some twenty-four hours following administration, it is quite obvious that one cannot hope to accomplish good by its use in acute collapse from avertin. Treatment with thyroxin prior to avertin administration is of such doubtful value and is accompanied by so strong a possibility of deleterious effects that it would seem inadvisable to employ this procedure.

Because insulin so greatly affects the utilization of carbohydrate, from which glycuronic acid arises, it was hoped that this hormone might hasten conjugation of avertin. Stamm's clinical observations[42] lend support to the hypothesis, the administration of adequate amounts of dextrose along with insulin seeming to shorten the period of unconsciousness from avertin. Lendle,[25] however, saw no shortening of unconsciousness in animals from insulin treatment; and Beck and Lendle[5] state that insulin does not hasten the disappearance of avertin from the blood when the anesthetic is injected at a constant rate.

The toxic action of avertin is exerted chiefly on the respiratory and vasomotor centers. Since there are available drugs capable of stimulating respiration and increasing vascular tonus, it is but natural that some of these should have been tried as avertin "antidotes."

Epinephrine is not only the most powerful vasoconstrictor substance available, but also exerts a definite influence on glycogenolysis. Beck and Lendle[5] state that epinephrine does not hasten the disappearance of avertin from the blood, but it is my opinion that this substance may be of service in some cases of sudden, profound avertin collapse. It should be borne in mind, however, that not only are there patients who are markedly susceptible to the action of epinephrine, but even when this susceptibility to the drug does not

exist, the abrupt rise in pressure following intravenous injection may bring on acute cardiac dilatation. The unfavorable results from the employment of epinephrine in chloroform poisoning[32] suggest, at least, the necessity for caution in utilizing it with patients under avertin anesthesia. Even when a favorable response occurs, the effects are of extremely brief duration, and are often followed by a definite reaction of depression.

Ephedrine, which, like epinephrine, acts peripherally to increase vascular tonus, is stated by Raginsky and Bourne[36] definitely to shorten the period of avertin narcosis in animals. They ascribe this not only to the improved circulation, but to a central action also; calling attention to the insomnia and nervousness not infrequently encountered in asthmatic patients treated with this drug. Their observations are in harmony with the antagonistic action of ephedrine against chloral hydrate observed by Airila.[1] Beck and Lendle,[5] however, state that ephedrine does not hasten elimination of avertin from the blood, and, from personal observation, the conclusion has been reached that ephedrine is very uncertain in its influence on avertin narcosis.

It would seem that caffeine has certain actions that would be of distinct service for overcoming avertin depression. In the first place, there is the well-known tendency of caffeine to cause insomnia, thus opposing the action of narcotic drugs. The respiration is improved; and, in normal animals, the extent of cardiac excursions is increased by the drug; and, as recently pointed out by Riesser and Brentano,[28] caffeine in large doses mobilizes hepatic glycogen. The use of caffeine in the treatment of poisoning by acetanilid,[18] alcohol,[34] or morphine[19] has, however, not only failed to give good results but been found often to lessen the chances of recovery. Beck and Lendle[5] did not observe any favorable response when caffeine was given to animals depressed by avertin; neither in the way of improvement of significant extent in the respiration or in the rate of disappearance of the anesthetic from the blood.

Interest in the employment of coramine for overcoming avertin depression was first aroused by the favorable report of Killian.[23] In 1924, Uhlmann[46] carried out a pharmacological study and concluded that coramine stimulates the medullary centers; respiration especially being affected. In overdose, coramine causes nervous hyperexcitability, terminating in convulsions; however, the margin between the effective dose and that sufficient to elicit these undesirable symptoms is unusually large. The efficiency of coramine as a respiratory stimulant has been confirmed by a number of other investigators. Asher[4] compared cardiazol with coramine on animals depressed by various narcotic agents, coming to the conclusion that the latter drug was superior for bringing about improvement in respiration and circulation and that its convulsant dose was some ten times greater than that of cardiazol. Schubel and Gehlen,[39] Helaers,[20] Gremels,[15] and Wieland and Mayer[48] all found coramine to be of distinct value for stimulation of the depressed respiration. In a recent communication, Maloney and Tatum[27] report the result of experiments in which caffeine, strychnine, cardiazol, and coramine were used in the treatment of poisoning by avertin and several other narcotic substances. Coramine proved not only to be the most efficient, but they are of the opinion that its use is much safer than is the case with the other drugs mentioned.

According to Uhlmann,[46] the isolated heart is stimulated by perfusion with solutions of coramine and when the drug is injected intravenously into intact mammals, there results a rise in the blood pressure and increased cardiac excursions. In the depressed animals used by Asher,[4] there occurred an improvement in the circulation as well as respiration. Guth[16] was able to demonstrate an increased blood flow under the influence of coramine in patients who had been subjected to

general anesthesia. Especially interesting are the experiments of Burgi and Gordonoff,[6] showing that coramine renders the heart more resistant to the action of depressant agents.

According to Killian, coramine is indicated both for overcoming acute collapse and also for shortening the duration of avertin narcosis. Results reported by other authors following the use of coramine for combatting collapse symptoms under avertin anesthesia have been distinctly favorable. Kennedy[22] used coramine in a considerable number of patients to relieve cyanosis or other mild evidences of undue depression from avertin, finding that doses of 2 to 3 c.c. intramuscularly produced uniformly good results. In two of his patients, a condition of apparent gravity followed administration of avertin; in both instances, coramine intravenously in relatively small dosage (1 to 2 c.c.) led to immediate improvement and subsequent recovery. Mörl's experience[30] was generally quite satisfactory; he reports one case of severe depression from overdosage with avertin where the intravenous injection of 2 c.c. and then of 3 c.c. seemed to have a life-saving action. Specht[41] reports a case where collapse resulted from the combined actions of avertin and morphine. The patient was deeply unconscious, pulseless, with dilated pupils and absence of reflexes. By the intravenous injection of two doses, each 5 c.c., of coramine intravenously, recovery could be effected. Schmidt[38] reports 2 cases where the patients were "practically dead" from the toxic action of avertin, but recovered after injection of coramine. Felix[11] encountered most severe collapse in a patient subjected to thyroidectomy under avertin anesthesia. The intravenous injection of 4 c.c. of coramine brought about dramatic improvement and recovery eventually occurred. Somewhat similar is the report of Osterweil,[33] Meyer[29] and Seemen[40] both noted a favorable action from coramine in patients with severe respiratory depression following avertin anesthesia. Jager[21] found that the intravenous injection of 5 c.c. of coramine failed to influence appreciably the respiratory depression encountered in a seventy-two-year old patient, upon whom thyroidectomy was being performed, but there was a question of mechanical interference with respiration from intrathoracic goiter. Kruckenberg[24] reports favorable results; as well as Domanig,[8] Fischmann,[12] Ruf,[37] Geiger,[13] Anschutz[3] and Treplin.[45] Killian is of the opinion that rather large doses of coramine should be employed in the cases of severe depression, as much as 15 c.c. intravenously. The effects are manifested within a matter of minutes after intravenous injection, but are apt to be transitory; because of this, it is advised that from 3–10 c.c. be injected intramuscularly in addition. In poisoning by other narcotic agents, also, good results have been reported following employment of coramine. Crohn[7] reports a "life-saving" action when coramine was used in the treatment of intoxication by phanodorn, luminal, morphine and barbital. His results have been confirmed by Glaeser[14] as regards luminal; by Altmann[2] whose patient had taken the enormous dose of 270 gr. of barbital; and by Ludwig and Hortnagel[26] who successfully treated a patient who had taken about 20 gm. of tincture of opium.

Only 2 cases of critical collapse were encountered in the present series:

One of these was a single female of forty-three years, subjected to hysterectomy. There was an interesting sidelight here, in that the patient was a firm believer in fortune-telling and had been told a week before hospitalization early in December that she or one of her two sisters was to be operated upon and would die before Christmas. The operation was relatively simple, being completed in twenty-eight minutes, and consisted in removal of the appendix as well as the hysterectomy. The patient left the operating room, apparently in good condition, and was given the customary dose of 2 c.c. of coramine subcutaneously. Within ten minutes, the interne was hurriedly summoned and found the patient in marked shock, with

imperceptible pulse and no sign of respiration. Epinephrine, carbon dioxide inhalation, and artificial respiration were given; to be followed as soon as possible by intravenous infusion of physiological sodium chloride solution. After about thirty minutes, 5 c.c. of coramine were injected intravenously. Spontaneous respiration set in and the color returned, but consciousness was not recovered. At three P.M., about seven hours later, there was still marked depression and deep unconsciousness. At this time, a second intravenous injection of a 5 c.c. of coramine was given, with the result that within the next three minutes, the patient awoke, with apparently normal faculties. In spite of this, however, the pulse remained very weak, and signs of shock persisted. Death occurred three days later.

The second patient had received no avertin, but was operated under spinal anesthesia with novol; the prostate being removed. About ten minutes after returning to bed, having left the operating room in good condition, he suddenly collapsed. Immediate intravenous injection of 5 c.c. of coramine resulted in return of color, improvement in pulse, and disappearance of the threatening condition. For the next seventeen days, the patient's condition was extremely poor, at times critical, and repeated injections of coramine in doses of 1 to 2 c.c. were given. Eventual recovery took place, the patient being in fairly good condition and able to walk on his discharge twenty-two days later.

These 2 cases furnish additional evidence as to the safety of rather large and of repeated dosage with coramine. In both instances, immediate improvement followed each administration of the drug and no undesirable effects were ever noted. Although the introduction of coramine into the veins results in exceedingly prompt action, the effects do not persist long, as noted by Killian[23] and others, and it is necessary in most cases to supplement the intravenous by subcutaneous or intramuscular administration. Indeed, it has been found that even orally coramine will usually produce definite effects within ten to fifteen minutes, and this method of administration may often be used to advantage. The relative persistence of the action of coramine given orally or subcutaneously is in marked contrast to the evanescent action of epinephrine.

Practically all authors agree that coramine exerts an awakening influence when given in sufficiently large dose to narcotized patients, but, while Killian is of the opinion that the duration of unconsciousness is shortened by the drug, others have contended that the effect is merely temporary; the patient soon lapsing back into a condition of unconsciousness. Beck and Lendle[5] find that the disappearance of avertin injected at a definite rate into the blood stream is not hastened by coramine, but this does not establish the correctness of the view that coramine fails to shorten the period of unconsciousness produced by avertin, because such an increase in excitability of the central nervous system may be brought about by coramine that a blood concentration of avertin, previously sufficient to cause unconsciousness, will now prove inadequate. Then, too, the improved respiration, the increased muscular tonus, and the acceleration of the blood flow would certainly seem to favor elimination of avertin that is actually in the blood. In the present series, it was noted, in agreement with Killian's observation, that, although the patients may appear to lapse back into unconsciousness after the first awakening from coramine, the sleep is much lighter and may easily be broken by stimuli previously ineffective.

A careful record of the time of return of consciousness in the 28 consecutive avertin cases preceding the use of coramine showed that an average of one hour and twenty-five minutes was required, as against an average of forty-eight minutes in the 82 patients where coramine was used after the avertin; a speeding up of recovery by thirty-seven minutes or 48 per cent. In agreement with this is the unanimous testimony of internes and nurses attending the patients in this series that the routine administration of coramine renders the postoperative condition of the avertin patients distinctly better as to color,

respiration and pulse quality than is the case with those which served as controls.

Further study is now in progress to determine the value of coramine in hastening recovery from ether anesthesia. It has seemed possible that the routine use of the drug here would hasten the return of consciousness even more than it does in patients given avertin, because of the fact that elimination of ether is accomplished largely through the lungs; and, consequently, would be influenced more by the improvement in pulmonary ventilation under the influence of coramine. Data are being collected, also, as to the incidence of pneumonia and atelectasis in coramine-treated patients, with the object of determining definitely whether this is lower than in a control series.

At the present time, from observations in 83 cases and from a review of the literature, the following conclusions seem justified:

1. Coramine is a definite stimulant to respiration and circulation depressed by avertin, novol, or in surgical shock.

2. The toxicity of coramine is low; so that large and repeated doses may be employed if the necessity exists. This is well illustrated in one of our cases, where 28 c.c. were given in a period of sixteen hours with apparently excellent results. Further, that in this series there was no evidence of depression after the immediate stimulation.

3. The use of coramine is suggested in all cases where early recovery from anesthesia, especially avertin-gas-ether sequence, is desired.

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TREATMENT OF PURPURA HEMORRHAGICA

REPORT OF 22 CASES*

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IT is my purpose in this paper to present 22 cases of purpura hemorrhagica and to discuss the results of treatments employed in this series of cases.

The term purpura hemorrhagica is used because it is descriptive and short. Among other common terms in use may be mentioned primary, essential or idiopathic purpura hemorrhagica, and thrombocytopenic purpura hemorrhagica.

Purpura hemorrhagica signifies a condition in which there are spontaneous hemorrhages beneath the skin, bleedings from mucous membranes and in some cases hemorrhages into some internal organ. It is associated with and accompanied by a marked reduction of blood platelets and a prolonged bleeding time. The red blood cells and the white blood cells show no changes of note except those that might be present because of hemorrhage.

There are many clinical entities in which purpura is only a symptom and in discussing the treatment of purpura hemorrhagica a correct diagnosis is of prime importance. This cannot be too strongly emphasized.

The criteria for a correct diagnosis used in this paper are:

1. Purpura, petechiae and ecchymoses.
2. Prolonged bleeding time.
3. Reduced number of platelets.
4. Positive tourniquet test.
5. Normal or slightly prolonged coagulation time.
6. Lack of primary disturbance of red blood cells or white blood cells.

This report is based on a study of 30 patients. Eight cases are not reported in this paper because no treatment was used. They represent cases in which recovery appeared to be spontaneous. The symptoms were never of such magnitude as to require treatment.

One person in this group is a female, aged fifty-eight years, with a history of recurring hemorrhages from the nose and gums over a period of twenty years. Her platelets vary between 40,000 and 80,000, her bleeding time is eight minutes and her clot does not retract.

The 22 treated cases comprised two groups:

1. Acute: 8 patients. Clinical course severe and progressive. Bleeding from four or more sites. Symptoms alarming. Duration usually over a period of less than six weeks. Hemoglobin 60 per cent or less.

Three of these patients were treated with repeated blood transfusions, 300 to 750 c.c. every twelve hours. All three died of hemorrhage in three to four days. A fourth patient died twenty-four hours after admission to the Hospital and eighteen hours after a 500 c.c. blood transfusion.

Splenectomy was done on 4 of this group of patients. Three died. One recovered and has been well over a period of three years. In this group, transfusions of blood were used before and after operation. It is of interest and importance to note that invariably the blood platelets reached a high normal, but the hemorrhages did not cease. One of these patients lived three days after splenectomy and during this time, bleeding from multiple sites continued in spite of repeated transfusions. In one person 2500 c.c. of blood were given in a period of three days.

2. Subacute: 14 patients. Symptoms over a period of four months or longer. Clinical course severe but neither progres-

* From the Department of Medicine, Long Island College of Medicine. Read before the Brooklyn Society of Internal Medicine, May 26, 1933.

sive nor alarming. Bleeding from less than four sites. Hemoglobin 70 per cent or better.

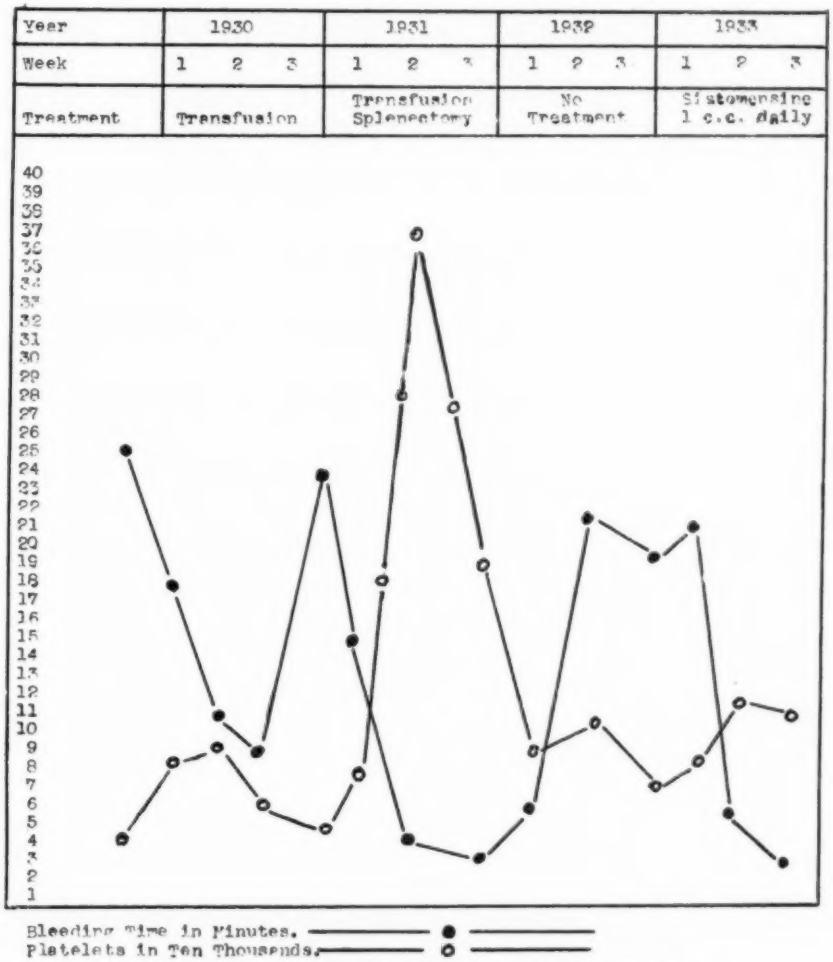

Fig. 1. Purpura hemorrhagica, Case 1. Ovarian extract.

Five of these 14 patients were treated by blood transfusions and splenectomy. Three of these recovered and have been well over a follow-up period of two for three years and one for two years. Two of these 5 patients treated by splenectomy suffered recurrence; one at the end of one year and the other at the end of two years. Five patients of this subacute group were treated by blood transfusions alone. At least three blood transfusions of 300 to 500 c.c. were used in each case. In some, as many as eight blood transfusions were given at intervals of one to four days. Of these 5 patients treated by blood transfusion alone, only one has had no recurrence over a period of two years. Four had a recurrence three to fifteen months after the last blood transfusion. Two of these were treated with Alpine light. Temporary improvement was noted. When symptoms recurred transfusions were used, bleeding did not stop and both patients died of hemorrhage. Splenectomy was refused.

Two of these four, recurring after blood transfusion, were treated with *x*-ray therapy over the spleen. One died of cerebral hemorrhage after the second treatment. The other remained well for a period of one year. During this time the blood platelets never reached above 100,000, the clot did not retract, but the bleed-

ing time fell from twelve to two and one-half minutes. This patient had a recurrence of symptoms and died suddenly after complaining of severe occipital headache. Both of these patients were in their third decade of life and had blood pressures of 160 to 180 mm. systolic and because of this unhappy ending in these 2 patients with purpura hemorrhagica and hypertension it is suggested that such patients be treated by splenectomy as soon as a diagnosis is established.

Five patients of this group of 14 sub-acute cases, 2 of whom had recurrences after splenectomy, were treated with 1 c.c. of sistomensine (5 rat units) per c.c. subcutaneously daily, for seven to twelve days. Three have had no recurrences. Two recurred in three to six months. Sistomensine was used and again the purpura as well as the bleedings from mucous membranes ceased.

TABLE I
PURPURA HEMORRHAGICA

Hosp. No.	Sex	Age	Bleeding Site*	Platelets	Bleeding Time	Coagulation Time	Clot Retraction	Tourniquet Test
4377	F	33	S.N.G.B.	44,000	13	10	*	****
1150	F	15	S.N.G.B.	50,000	10	8	0	****
3509	F	30	S.N.V.G.B.	72,000	180	6	0	****
3702	F	22	S.N.V.G.	65,000	11	4	0	***
1664	F	47	S.V.G.	75,000	18	8	0	***
2021	F	54	S.N.V.G.	36,000	9	8	*	***
6130	F	16	S.N.V.B.	40,000	45	3	0	****
597	F	37	S.N.V.G.B.	20,000	22	3	0	****
3935	F	15	S.N.V.G.B.	30,000	65	6	0	****
1266	F	45	S.N.G.B.	25,000	22	5	0	****
2537	F	43	S.N.G.B.	30,000	28	8	**	***
3601	F	16	S.N.V.G.B.	1,200	30	9	0	****
8427	F	42	S.N.V.G.B.	14,000	120	6	0	****
7123	F	45	S.N.V.G.	85,000	28	8	**	***
2305	F	25	S.N.V.G.	40,000	19	6	*	***
1618	F	33	S.N.V.	90,000	38	7	*	****
2305	F	55	S.N.G.B.	18,000	40	8	**	****
1618	F	38	S.N.V.	76,000	60	10	0	***
6402	F	35	S.N.V.G.	36,000	19	12	0	***
4638	F	42	S.V.G.B.	28,000	15	8	0	***
2506	F	17	S.N.V.G.	60,000	22	9	0	****
2304	F	19	S.N.V.G.	48,000	18	8	*	****

ABBREVIATIONS. *S, Skin. N, Nose. V, Vagina. G, Gums. B, Bowel.

TABLE II
PURPURA HEMORRHAGICA:
RESULTS OF TREATMENT

	Transfusion	Splenectomy	Alpine Light	*X*-ray	Glandular Therapy
No. of cases	5	9	2	4	5
Recovered	1	5	0	0	3
Recurred	1	2	1	2	2
Died	3	2	1	2	0

The specific cause of purpura hemorrhagica is not known. Occasionally, infection seems to account for some cases; others are thought to be manifestations of allergy and more recently attention has been drawn to possible vitamin deficiency causes and to disorders of glands of internal secretion.

Since 1883, when Hayem[1] first described blood platelets, a reduction in these blood

[1] Hayem, G. Leçons sur les maladies du sang. Paris, 1900.

elements has been held responsible for the hemorrhagic manifestations occurring in purpura hemorrhagica. However, although a reduction of blood platelets nearly always occurs in purpura hemorrhagica, the mere reduction in platelets is not the essential factor in the production of hemorrhages.

Rosenthal[2] in a complete and elaborate classification of all the purpuras emphasized the variability of the number of platelets and the lack of an absolute proportional relationship between the hemorrhagic manifestations, the number of platelets, the clot retraction and the bleeding time. Furthermore, after splenectomy there usually occurs a marked rise in platelets which may soon fall to an extremely low number without the recurrence of hemorrhages.

The experimental work of Bedson[3] has thrown some light on this phase. He found that the injection of serum agar into animals reduces the platelets to a low figure but does not produce hemorrhages. If, however, an anti red cell serum is injected four hours previously, the subsequent injection of agar serum rapidly produces purpura. Bedson suggests that the anti red cell serum injures the capillary endothelium which is closely related genetically to the red blood cells. Normally in such a case the platelets would be deposited on the injured areas and act as protective agents, but if the platelets have been previously destroyed (by agar serum) the damaged capillary endothelium is left unprotected and hemorrhage results. Abnormal capillary permeability to blood may then be the initial disorder of purpura.

[2] Rosenthal, N. The blood picture in purpura. *J. Lab. & Clin. Med.*, 18: 303, 1928.

[3] Bedson, S. P. The effect of splenectomy on the production of experimental purpura. *Lancet*, 2: 1117, 1924.

The platelets are reduced in number secondarily, as they are used up to defend the weak areas. If the capillary damage is slight the platelet count falls, but the defensive work has been satisfactorily carried out. If the endothelial damage is widespread all the platelets may be used up without supplying adequate protection and severe hemorrhage occurs. So that capillary weakness or hyperpermeability may be the outstanding factor in the production of the symptomatology of purpura hemorrhagica. The rôle played by the spleen is not clear. Bedson found that splenectomy in guinea pigs protects against the production of experimental purpura.

The pathogenosis of purpura hemorrhagica may be hypothecated as follows:

1. Unknown factor: infection toxin, endocrine vitamin leading to
2. Increased permeability of capillaries, which results
3. In purpura.
4. Platelets are reduced because they are used in repair of endothelium.
5. A low platelet number plus increased permeability of capillaries leads to mucous membrane hemorrhages.

CONCLUSIONS

1. Twenty-two patients with purpura hemorrhagica were treated by:
   (a) Blood transfusion alone.
   (b) Blood transfusion and splenectomy.
   (c) Alpine light.
   (d) *X*-ray.
   (e) Ovarian extract.
2. Recurrences occurred regardless of the treatment used.
3. Splenectomy gave good results in 77 per cent of the patients so treated.
4. Five patients, 2 with recurrences after splenectomy, responded well to treatment with ovarian extract.

LYMPHOGRANULOMATOSIS VENEREA*

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EPIDEMIC inflammation of the inguinal lymph nodes has been described in different countries under such names as subacute inguinal lymphadenitis, epidemic inguinocrural adenopathy, inguinal lymphogranulomatosis, etc. This multiplicity of denominations is due, we believe, to the confusion that exists as regards the true cause and symptoms of this disease, which is very often mistaken for the common lymph-node syndromes.

Chassaignac (1859), Velpeau (1865), Jouet (1886), Guérin (1887), Nélaton (1890), Brault (1894), Marion and Gandy (1901), Pigeon and Tanton, etc. described simple forms of subacute lymph node inflammation with intraganglionic suppurative foci, which, according to Hellerström, had been observed during the eighteenth century and attributed an African or American origin (Freis). Only in 1913 did Durand, Nicolas and Favre point out the true epidemic nature of this condition, awarding it the importance of a new disease and describing its principal symptoms and evolution.

Since 1926 we have observed among us some cases of inguinocrural or deep iliac lymph-node inflammation, which occurred with greater frequency during Spring and Summer in 1929–1930. During the same seasons of 1930–1931, and 1931–1932, the number of patients suffering from these conditions increased greatly, and they acquired the character of an epidemic.

During these last periods we studied 82 cases, all of them in men, of subacute inflammation of both inguinocrural and deep iliac lymph nodes, which resembled each other closely in some symptoms but differed substantially in others. We will refer only to those in which no external lesion could be found that would explain the inflammation of the regional lymph nodes.

After observation and careful study of these cases and others referred by several colleagues, although we do not wish for a moment to diminish the importance of previous investigations on this subject, we do not believe that all conditions which fall under Durand, Nicolas and Favre's denomination are one and the same disease, a fact which we have already discussed in a previous article.[1] This same point of view has also been lately sustained by Gougerot and Cohen.

ORIGIN

According to Hellerström the epidemic that appeared in Europe during the eighteenth century was assumed to be of African or American origin. We are not capable of discussing the former possibility but as regards the latter we shall refer to and discuss certain bibliographical investigations we have carried out.

Father Bartolomé Las Casas, who crossed from Spain with the early conquerors of the New World, described a disease transmitted through sexual intercourse by Indian women to Spaniards, which was called "bubas," and about which López de Gomara said:

> The inhabitants of this "Isla Española" all suffer from "bubas," and as the Spaniards held sexual intercourse with Indian women, very soon they swelled with "bubas," a very contagious disease, that produces intense pain. Ailing and not curing, many of them returned to Spain.[2]

Oviedo de Valdes gives more or less the same description of this disease[3]; William Pison,[4] describing the diseases of Brazil,

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refers to a contagious ailment not only transmitted through sexual intercourse, but also through the slightest contact, which he believes endemic to the country and that was called by Spaniards and Portuguese "bubas." This disease, according to the author, is very different from the "mal français."

Other writers such as Pedro Cieza de León,[5] Jacob Le Moyne,[6] and Rodrigo Diaz de Isla, refer largely to venereal diseases acquired in the New World, but their descriptions of the principal symptoms make us believe that they confused syphilis, soft chancre, lymphogranulomatosis and leishmaniosis.[7]

Numerous authors of the sixteenth and seventeenth centuries, who described venereal diseases, made special reference to simple buboes, that show no relation with ulcerations of the external genitalia. Astruc in his "Treatise on Venereal Diseases"[8] says:

> Three types of buboes can be distinguished, according to the cause that produces them: some are due to impure commerce and then it is an essential disease; others are produced after virulent gonorrhea has been suppressed or following ulcerations of the penis, then it is a symptomatic disease; others appear spontaneously, bad sexual intercourse being very distant, then it is a pathognomonic sign of some occult venereal disease.

Swediaur, Gilbert and Beaumés, Vidal de Cassis, etc., also refer to this primitive buboe (d'emblée) and Cuzco, quoted by Belhomme and Martin[9] sustains that in certain cases a primary lesion of the genital organs may be absent in the same way that many initial evidences of infectious diseases fail to appear. Belhomme and Martin, on the basis of facts pointed out by De Castelnau (penetration of syphilitic virus without previous ulceration of the genital organs[10]) believe that in the case of this primary buboe things may happen in the same way. From what numerous writers of the eighteenth and nineteenth centuries say, it would appear that this type of simple buboe is common in tropical regions; both sailors and soldiers seem to have been especially predisposed to it. In

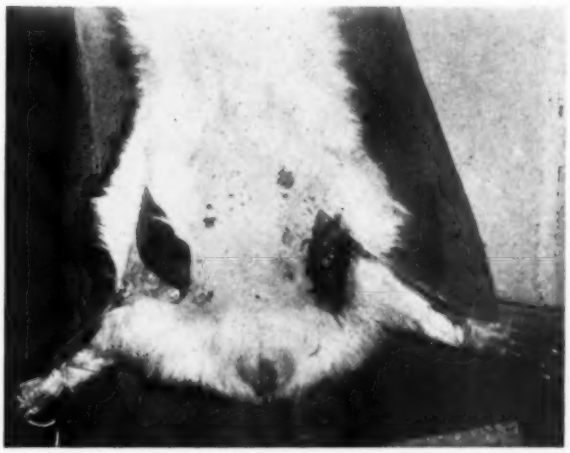

Fig. 1. Experimental lymphogranulomatosis venera, five days after inoculation of virus from brain substance of rabbit. Left inguinal lymph nodes, showing foci of necrosis and intense periadenitis.

1886 Jouet and in 1887 Guérin refer to this condition as "ganglion de fatigue de soldats colonials"; Ruge observed this disease among sailors of the Italian navy in South America, and Goding, among members of the British Navy stationed on the West Coast of Africa.

From the descriptions by the writers of the fifteenth and sixteenth centuries of the different diseases transmitted to Europeans through sexual intercourse with Indian women of the New World, we arrive at the definite conclusion that not only did they acquire syphilis but also yaws, leishmaniosis, soft chancre, as well as lymphogranulomatosis. The natural confusion arising at the time is easily explained, owing to the total absence of bacteriological knowledge. Nevertheless we find such marvellous and detailed descriptions of symptoms, that with our present knowledge of these diseases differentiation is easy.

ETIOLOGY

Notwithstanding all that has been done and investigated, the determining agent remains up to the present unknown. As

regards the mode of infection, we also participate in the general opinion that it is through sexual intercourse.

after this period the lymph nodes subside gradually. Microscopical examination of sections of these lymph nodes reveals an

Fig. 2. Inguinocrural lymph-node inflammation; genital lesion of meatus. Dark field investigations negative. Autoinoculation, Reenstierna. Wassermann and Kahn reactions negative.

Fig. 3. Lymphogranulomatosis venerea, twenty-two days after ganglionar inflammation appeared; absence of genital lesion. Weakly positive Frei's reaction. Wassermann and Kahn reactions negative.

Freund and Reis, Meyer, Rosenfeld and Anders have recently been able to reproduce the disease experimentally in guinea pigs and rabbits; lately Levaditi and collaborators were able to isolate an invisible virus from the brain of experimentally infected monkeys (Macacus cynomolgus) and white mice, which, once inoculated under the prepuce of general paretics, developed in them a ganglionic condition resembling the initial stages of Nicolas-Favre's disease. Most of these authors, and especially Levaditi and Anders, have described typical macroscopical and microscopical changes in lymph nodes and brains of animals experimentally infected with this virus.

We have also been able to obtain, by means of subcutaneous injection of material from human lymphogranulomatosis, an increase in size of the inguinal and lumbar lymph nodes in guinea pigs. The highest stage of growth is reached between the sixth and eighth day after inoculation; increased vascularization congestion and a certain number of cells in piknosis, but none of the typical lesions described by Meyer, Anders and Levaditi; notwithstanding this fact, most of these inoculated animals present a positive Frei reaction. We have not found nodes in the liver, lungs or spleen as described by these authors.

By means of intracerebral inoculation in white mice of human material as well as from inoculated guinea pig lymph nodes, we have failed to reproduce the typical lesions described around meningeal and cerebral blood vessels. Nevertheless by subcutaneous injection of the brain substance of these mice into guinea pigs, we have obtained, conjointedly with Onetto, who proposed this technique, a considerable increase in the size of inguinal lymph nodes between the sixth and eighth days after inoculation. Microscopical examination of these lymph nodes shows similar changes to those already described. Control animals inoculated with brain sub-

stance of normal white mice, showed only a very slight increase in the size of the lymph nodes.

increase in size of the lymph nodes to secondary infection, owing to the fact that such lymph nodes when broken down and

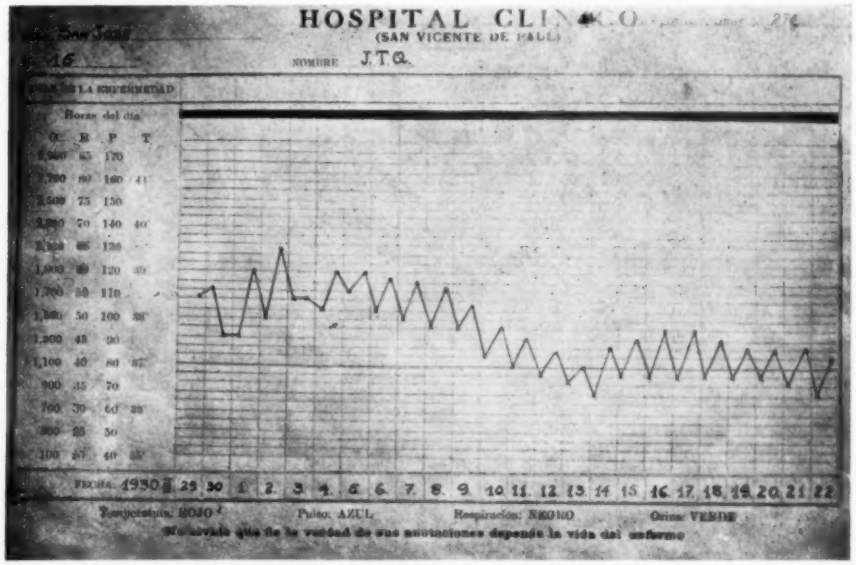

Fig. 4. Temperature curve of patient that entered hospital fourteen days after appearance inguinoiliac lymph node inflammation has set in, with arthritis of right wrist. During sojourn he developed arthritis of left knee and right ankle. Eosinophiles 5 per cent; lymphocytes 27 per cent; neutrophile polynuclears 63 per cent.

Intracerebral inoculation of brain substance of experimentally infected white mice into young rabbits activates the virus; subcutaneous inoculation of brain substance of such rabbits into guinea pigs produces between the fourth and fifth days a very considerable increase in the size of the inguinal lymph nodes. The virus after its passage into the brain of young rabbits reaches its greatest virulency between the ninth or tenth days after inoculation. Controls inoculated with the brain substance of a normal rabbit showed only a slight swelling of the inguinal lymph nodes.

Reinoculation of guinea pigs previously infected with material from human lymphogranulomatosis or with the brain substance of rabbits infected with virus from the brain of white mice, does not cause a new swelling of the inguinal lymph nodes.

Although we have not been able to demonstrate microscopically what other investigators estimate as typical changes in the lymph nodes and brain of experimentally infected white mice and monkeys, and as in our case we cannot attribute the cultured in different media proved sterile, we believe that microscopical findings ascribed to experimental lymphogranulomatosis must not be considered as conclusive evidence of the disease, a fact which up to the present holds good for human lesions where no typical alterations can be distinguished in the diseased lymph nodes.

A question that naturally arises after what has been said is: where is the origin of this virus? With the object of enlightening our knowledge as regards this question we have tried, in every case that has come under our observation, to carefully investigate the possible sources of contagion, and as all our cases have been registered in men during active sexual life, we logically had to suppose that the infective agent was harbored in the female genital tract. But we had not registered any such cases in women and moreover several patients for months previous to the appearance of general or local symptoms had practiced only "coitus buccalis" in order to evade venereal disease contagion.[11]

This last fact, pointed out by us, has also been recorded lately by several other colleagues.

Name	Age	Wassermann Reaction	Kahn	Soft Sore	Adenitis	Frei	Reens.	Control	Eos., (Per Cent)
B. S.	23	++	+++	.....	.....	+	+	−	0
H. S.	25	+	+++	.....	.....	+	+++	−	1
M. D.	24	−−	−−	.....	.....	+++	+	−	0
R. M.	20	−−	−−	.....	.....	+	−−	−	0
M. V.	34	−−	−−	.....	.....	+++	−−	−	2
T. M.	30	+++	++++	.....	.....	+	−−	−	0
T. S.	21	+	−−	.....	.....	+	−−	−	1
O. M.	28	−−	−−	.....	.....	++	−−	−	0
A. G.	29	−−	−−	.....	.....	+++	−−	−	1

In all women who were considered as the source of contagion and who could be examined, no open lesion could be found in the external genitalia, vagina or cervix.

Our previous studies on soft chancre had showed us the great difference in the frequency of this condition between men and women (20 to 1) and we had also been able to establish that in certain cases soft chancre developed in men who had held sexual intercourse with a known woman, who on examination showed no infective lesion. The absolute certainty of the nature of this sore was established both by isolation of the streptobacillus of Ducrey-Unna and a positive Reenstierna reaction.

Women who were considered as infective agents of lymphogranulomatosis or soft chancre and who came under our observation, were tested for Frei and Reenstierna's reactions, but in all cases these were negative. Subdermal inoculation of vaginal secretion failed to reproduce an experimental soft chancre.

We next performed both these allergic reactions in 250 normal women, who on examination presented no external lesion of their genitals, vagina or cervix.

The results obtained were negative in 241 (96.4 per cent) and positive in 9 (3.6 per cent) as regards Frei's reaction. Out of the 9 women with a positive Frei reaction, 4 had an intensely positive reaction, and both Wassermann and Kahn reactions negative. Only one had a slightly positive Reenstierna reaction. Of the remaining 5 that presented a weakly positive Frei, 3 had an intensely positive Kahn reaction; one a very intense, another a weak Reenstierna reaction (Kitchevatz, Franchi, de Gregorio i Serrano, Favre). None of these women had ever observed any lesion of their external genitals, nor suffered previously from adenitis.

On the evidence of the facts we have been detailing, we believe that the female genital tract harbors, under conditions at the present time undetermined (variation in pH?), pathogenic microorganisms in a latent stage, that once transferred to optimal conditions recover their primitive virulence and cause disease.

According to our opinion the virus that produces lymphogranulomatosis is of buccal origin.[12] We have sufficient clinical

evidence to sustain this theory and also to declare that the increase in the number of cases of this disease is due, in our opinion, to the greater frequency with which coitus buccalis and cunilinguism is practiced at present, owing to circumstances directly related to the restrictions in childbirth, fear of fecundation or venereal contagion.[13]

The practice of coitus analis, which every day is becoming more frequent, as a medium of preserving libidus without fear of fecundation, is responsible, in our opinion, for those undefined chronic inflammations and strictures of the rectum, hard infiltrations of parametrium, etc., just recently allied to Nicolas-Favre's ganglionic syndrome (Jersild; Nicolas, Favre, Massia, and Leveuf).

Sénèque in the clinic of St. Louis Hospital, Paris, was able to establish in certain such cases that came under his observation an intimate relationship between this condition and sodomy. Barthels and Biberstein point out the greater frequency of such rectal lesions in women and quote the statistics of Berg (103 women, 15 men), Pölscher (190 women, 25 men), and Ruge (61 women, 2 men), to prove this statement. Bensaude and Lambling also describe and study 21 such cases in women, with a positive Frei reaction.[14]

Contemporaneous sexual paganism, restricted social conditions and poverty place us nowadays face to face with a new pathology, which will reveal to us all its mysteries only when we grant these factors their true value as determining causes of new syndromes and disease.

SYMPTOMS

The onset of the disease speaks in favor of a systemic invasion. The length of the incubation period is up to the moment undetermined. A few days before the swelling of the lymph nodes appears, the patient suffers from anorexia, slight headache, dorsolumbar pains, arthralgia and general discomfort. The inflammation of inguinocrural and deep iliac lymph nodes starts some days afterwards, and sets in gradually. First a slight, hard, unpainful swelling of one or several inguinocrural lymph nodes appears and on deep palpation of the iliac fossa we can elicit a similar condition of the deep iliac lymph nodes. No lesions can be found on the skin of the external genitals, nor ulcerations around or ôn the surface or deep zones tributary to the affected lymph nodes.[15] There is slight fever and joint pains increase. Eosinophilia is constant.

During the second week, inflamed lymph nodes reach their maximal growth; fever increases and is persistent throughout the day. Both spleen and liver appear enlarged (Ravaut); poligangliosis (Todd, Chevallier and Barreau) and intense inflammation of the epitrochlear and cervical ganglia may be present (Ravaut).

There is tenderness on deep abdominal palpation, especially around the umbilical region, due, we believe, to concomitant inflammation of mesenteric or lumboaortic lymph nodes. In certain cases arthritis appears, even with hydrarthrosis. In one case, that of a colleague of ours, arthritis appeared before the lymph nodes swelling.

With the occasional exacerbation of some of the aforementioned symptoms the disease develops its course, lasting in some cases as long as three months. During its evolution we have observed in some cases symptoms of severe sepsis: high fever, intense prostration and albuminuria.

In order to convey a clearer impression of the different symptoms we will analyze certain of them separately.

Arthralgia is a constant symptom. It sets in with prodromes of the disease and persists during the first three weeks, with occasional exacerbations. Nicolas and Favre describe some cases that resemble rheumatism. Pains are more frequently experienced in the wrists, knees and ankles. Fernandez de la Portilla attributes these arthralgias to the administration of antimony, but we differ from his opinion, as they appear before treatment is started and are also present in cases that have

not been submitted to the action of this metal.

Arthritis is not very common; in one case we observed its appearance in the right ankle several days before any ganglional inflammation appeared.

Its principal characteristic is its fugacity. Starting suddenly, it is accompanied by all the typical symptoms of acute joint inflammation and resembles objectively a case of gonorrheal arthritis. One or two days after its onset, normality is recovered with the same rapidity. In some cases we have seen as many as three different joints affected at different periods. Twice we have been able to establish the coexistence of intra-articular effusion. Buschke, Boas and Vásárhelyi allude to a case accompanied by severe sepsis and multiple arthritis.

Eosinophilia is a very constant finding; it can be evident early in the disease and persists for a long time after the general symptoms have disappeared and ganglionic inflammation has almost totally subsided. Vicuña in his series of 9 cases found from 2 to 23 per cent eosinophiles in the blood of his patients. Ravaut and his collaborators sustain that eosinophilia is not constant and when present is very slight; according to them there is a predominance of small and large mononuclear cells in relation to neutrophile polynuclear cells (33 per cent) and lymphocytes (1 per cent).

Inflammation of the inguinocrural and deep iliac lymph nodes sets in gradually. The lymph nodes are hard and not painful. Periadenitis may set in early, but usually it appears after the first fortnight, when we can also demonstrate fluctuating zones in the diseased ganglia.

So far we have not observed the spontaneous ulceration of lymph nodes; after the height of the inflammation has been reached, they gradually and slowly recede, acquiring a hard, scirrhous consistency which sometimes persists for several months after all other phenomena have totally disappeared.

In the 32 cases of this symptom complex, where no point of inoculation could be established in the tributary regions of inflamed lymph nodes, the frequency with which the different symptoms appeared was as follows: fever 100 per cent; arthralgia 100 per cent; inguinocrural and deep iliac lymph-node inflammation 100 per cent (double 62.5 per cent); eosinophilia 93.7 per cent; enlarged liver 90.6 per cent; enlarged spleen 87.5 per cent; abdominal pain 43.7 per cent; headache 37.5 per cent; epitrochlear lymph-node inflammation 18.7 per cent (in 4 out of these 6 cases, the Kahn reaction was positive); arthritis 18.7 per cent; polygangliosis 9.3 per cent (in one of these 3 cases, the Kahn reaction was positive).

Direct relationship between coitus buccalis and the disease could be established in 8 cases (25 per cent).

DIAGNOSIS

The beginning of the disease, its general prodromes, may induce us at first to believe in the possibility of an attack of mild grippe or in the onset of some common infectious disease. Once the lymph nodes become involved, the clinical entity defines itself clearly; the successive appearance of some or most of the symptoms described and the presence of a persistent eosinophilia confirm the diagnosis.

Frei's reaction has been allotted great importance as a means of establishing the diagnosis. Of the 32 cases of lymphogranulomatosis that we have carefully studied and in which no apparent site of inoculation could be established in or around the zones tributary to the inflamed lymph nodes, this reaction was positive in 22 (68.7 per cent) of the cases. Eight (36.3 per cent) among these had positive Kahn reactions and 6 (27.2 per cent) a concomitant positive Reenstierna reaction. Frigolett in 6 similar cases, with no previous venereal antecedents, found in all of them a positive Frei reaction.

Investigating Frei's reaction in patients suffering principally from genitourinary diseases, who attend our public dispensaries in Santiago, we obtained the

following results: total of men submitted to the test, 97. Of 54 suffering from gonorrhea at different periods, 4 had a positive Frei reaction; one of these was a malaria case and another had suffered in 1930 from an inguinal adenitis of undetermined nature. Fourteen patients suffering from syphilis either in the primary or secondary stages all had negative Frei reactions, as well as 2 patients with latent syphilis who were tested. Of 10 patients suffering from soft chancre, all had a negative reaction. Out of 7 cases of inguino-iliac lymph-node inflammation with no apparent site of inoculation, 4 had a positive Frei reaction; 3 of them also had a positive Kahn reaction. Out of 6 cases of the same type of lymph-node inflammation, with an external genital lesion and repeated negative dark field examinations, 3 had a positive Frei reaction and all 3 had negative Kahn reactions. Six similar cases studied by Frigolett all had positive Frei reactions and in 3 cases there was a concomitant positive Wassermann reaction.

Of the 4 remaining cases of our series, a patient who suffered from scabies had also a positive Frei reaction.

Summarizing we observe that among the 84 patients that had no lymph-node inflammation 5 (5.8 per cent) presented a positive Frei reaction; among the 13 that suffered from inguino-iliac inflammation, 7 (53.8 per cent) had a positive reaction.

As regards women, 54 patients attending our public dispensaries were tested with the following results: out of 19 that suffered from genital gonorrhea in any of its forms, 3 had a positive Frei reaction. Two of these patients suffered from chronic anexitis. All 3 had negative blood tests. Seven women suffering from active syphilis all had negative Frei reactions; of 19 that had latent syphilis, serologically established, 4 cases presented a positive intracutaneous reaction. Of the remaining 9, only one that suffered from esthiomena vulvae had a positive reaction. In this case both Wassermann and Kahn reactions were negative.

Summarizing all the cases investigated we observe that among the 54 women who suffered from no inguino-iliac lymph-node inflammation, 8 (14.8 per cent) had a positive Frei reaction.

Twenty children under ten years of age who were tested with lymphogranulomatosis antigen, all reacted negatively.

Judging from our experience and that of several other authors (Vicuña, Gougerot, Cohen, etc.) it appears that Frei's reaction is not constant and therefore not strictly specific, a fact that allows us once more to sustain that, in our opinion, Nicolas and Favre's disease includes cases that differ from the classical description made by these authors.

Differential diagnosis must be made in the first place from inflammation of the inguino-iliac lymph nodes where a definite site of inoculation can be established. In this variety, ganglionic inflammation that affects only one side, starts several days after one or several ulcerations of the balanic region, preputium, or urinary meatus have made their appearance. Dark field examination of these lesions is always negative. In some cases we have only observed the presence of a slight urethral discharge. In several of such cases that have come under our observation we have been able to establish without any possible doubt a direct relationship between coitus buccalis and the appearance of genital ulcerations. Lymph nodes increase slowly in size and show a marked tendency to suppurate and open spontaneously, with the establishment of fistulae. Fever and general malaise accompany the lymph-node inflammation, but do not precede it. Eosinophilia, when present, appears late, is transient and not very marked (3–4 per cent); there is more often a mononucleosis with lymphopenia.

Chronic suppuration of inguinal lymph nodes due to Ducrey bacillus infection can be easily demonstrated by means of Reenstierna's reaction. In case of doubt, autoinoculation is definite.

Tuberculosis of inguinal lymph nodes has in certain cases a marked resemblance to lymphogranulomatosis venerea. In a patient suffering from genitourinary or pulmonary tuberculosis there is no difficulty in establishing the true nature of the ganglionic syndrome. Numerous authors believe that lymphogranulomatosis venerea is due to the action of Koch's bacillus or its toxins (Paltauf, Sternberg, Gortchakoff, Gay Prieto, etc.); this theory has been proved to have no basis (Vasiliu).

In countries where plague is endemic, it is necessary always to bear in mind the possibility of unapparent cases of the disease. Nevertheless microscopically there exists no similarity between lymphogranulomatosis and plague buboes (Gastinel and Reilly).

Fischer, Frei and Hellerström have confirmed the hypothesis of the identity of lymphogranulomatosis venerea and climatic buboe and Geisler refers to their common characteristics.

CONCLUSIONS

After careful clinical observation over several years of numerous cases of ganglionic syndromes, we believe that there exist two different diseases, whose symptoms have so far been misinterpreted and mixed with each other.

In one we find a definite site of inoculation in the genital organs, and a ganglionic syndrome of unknown nature. In the other we have a general disease, of unknown nature, preferably located in lymphoid tissue, especially in the inguinal, deep iliac, mesenteric and lumbo-aortic lymph nodes and where no definite site of inoculation can be established.

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5. Cieza de León, P. Crónidel Peru. 1st. part, chap. xlvi.
6. Mentioned by Julian Palmarius: Lue venera, Book i, chap ii, 1578, as referring to venereal buboes acquired through sexual intercourse with menstruating Indian women of Florida.
7. There is no doubt that certain cutaneous lesions recorded in Incassic figure pottery correspond to leishmaniosis.
8. Ed. Marin, Span. trans. Madrid, 1772, 3: 199.
9. Tratado práctico i elemental de patalogiá sifilítica i venéréa. (Spanish transl.) Madrid, 1878, pp. 73–79.
10. Feldman demonstrated experimentally that spirochaetes can pass through normal and intact skin and mucous membranes (*Klin. Wchnschr.*, p. 388, 1928).
11. Very few cases have been described in women and among these we will mention as of special interest, one presented by Louste and Thibaut at the meeting held on July 12, 1923 by the Société francaise de Dermatologie et de Syphilologie.
12. Wehrhein described a case of lymphogranuloma inguinale in which the origin could be related to a buccal coitus; Buschke observed a case of lymphadenitis of the neck; the initial lesion appeared in the tongue and was due to abnormal sexual intercourse.
13. During my visits to the Incassic Museum of Lima (Peru) I had the opportunity of examining numerous samples of pre-Columbian Incassic pottery ("huacas"), representing scenes of coitus buccalis, coitus animalis, cunilinguism and sodomy.
14. Meeting of Dec. 12, 1931, Société de Biologie, Paris.
15. Dr. Diaz Muñoz communicated to us that in one of his patients he observed the appearance of herpes genitalis five days after inguino-iliac lymph-node inflammation had started. This patient had only indulged in coitus buccalis; he was engaged to be married and practiced this form of sexual relationship from fear of venereal disease contagion.

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CHOICE OF PROCEDURE IN CASES OF PROSTATIC OBSTRUCTION*

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SOME of the recent contributions on the subject of prostatic hypertrophy, particularly those relating to cystoscopic resection, have, in a measure, reopened the whole subject of prostatism and prostatectomy. For a period of several years before this new era, sporadic papers appeared here and there but they often seemed a bit trite. Meetings, such as this one, covering a period of three or four days, would often assemble and disperse without a word on the subject. In other words, with the exception of a few perhaps minor technical variations, we were all pretty much in accord. The great majority of operators throughout the country were employing more or less as a standard procedure the two-stage suprapubic operation; a few, notably Hunt while at The Mayo Clinic, favored the one-stage suprapubic procedure, feeling that the better visualization meant more accurate control of bleeding and an added factor of safety. Young and a few others, mostly those trained under him, were doing most of their cases by the perineal route and showing perhaps better mortality statistics than any of us. Caulk was standing bravely and practically alone with his cautery punch. And may I say in passing that when the last word is finally said on the subject of cystoscopic resection and we are trying to give credit where credit is due, the name of John Caulk will loom large on the list. The merit of any surgical procedure stands or falls not so much on technical variations as it does upon the proper appreciation of the underlying pathological condition. I believe that Caulk has based his attitude upon a proper appreciation of this factor and to that extent has been right. I shall discuss this point a little more at length later on in my paper.

However, I repeat, with a few minor technical variations, we were all more or less in agreement. We had all of us seen and perhaps taken a small part in the gradual evolution of these problems. We had seen the frightful mortality and morbidity of the early days of the present century reduced to almost a negligible factor, largely because of painstaking attention to the details of selection, preparation and after care of our cases rather than to any increase in skill or improvement in operative technique. In other words, we were gradually settling into an attitude of smug complacency, which of course was not a healthy attitude.

In the last few years we have had presented to us: accurate suturing of the bladder neck following suprapubic enucleation; one-stage suprapubic prostatectomy with complete closure of the bladder without drainage as suggested by Lower, radical resection of the bladder neck for fibrotic prostate as suggested by Crabtree, and finally, and perhaps most dramatic of all, the cystoscopic resection of all types of prostatic obstruction as so ably advocated by Davis, McCarthy and others. These contributions, all of them extremely valuable, have, as I say, reopened the whole subject and brought about a thoroughly healthy and desirable state of affairs. When these newer methods have been properly evaluated and have been subjected to the acid test of time they will, of course, inevitably gravitate to their proper places as more or less important additions to the armamentarium available for handling this important group of cases.

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All of these recent contributions, particularly those dealing with cystoscopic resection, have been tinctured by the enthusiasm of their advocates. I say this in no spirit of criticism but as a statement of a logical and commendable fact. No forward step can be taken unless it is backed by a high degree of enthusiasm on the part of its advocates.

This would seem an appropriate time to take stock of our present position. It would seem, too, appropriate that this task might be modestly undertaken by an average urologist (which I like to consider myself) working in an average clinic, obtaining average results and entertaining no brief for any particular plan of procedure. I am basing my paper, as I also base my present attitude, in part upon a study of 125 consecutive cases recently admitted to my clinic (covering approximately the period during which cystoscopic resections have become popular), in part upon a careful study of the recent literature and in no small measure upon a more or less philosophical contemplation of the whole problem, growing out of a professional lifetime spent in urological work. May I at this time state my attitude, which is the most important point, perhaps the only point in my paper. I believe that we should make every effort, and now particularly when we have so many weapons at our command, to fit our procedure to the particular requirements of each individual case, rather than fit the patient to the operation. This sounds like a very trite statement and it might well be said that there can be no argument on that score. This is freely admitted and yet in actual practice how often does it happen that the most obvious things are apparently overlooked.

The choice of procedure in cases of prostatism depends upon several factors, first and foremost of course upon the fundamental underlying disease: the type and character of obstruction. There are, however, numerous other factors of almost equal importance which enter into the problem in many cases, such as the degree of obstruction, the absence or presence and degree of infection, the amount of discomfort existing, the age and general physical condition of the patient, his economic status, his habits, his occupation and even the location in which he lives. All or any of these latter items may be the deciding factor in determining whether a given patient should be subjected to any form of operative treatment.

In my group of 125 cases recently studied (excluding cases of carcinoma) in all of which the patients were admitted to the hospital for probable operation, there were 16 upon whom no form of operation was done; one because he was moribund, 2 because their various tests, which are ordinarily employed, did not measure up to required standard of operability, 4 who were operable but refused operation and 9 others who were perfectly good operative risks and requested operation and yet who in our opinion could be maintained perhaps indefinitely in comfort without any form of surgery. I see many other patients in my office (not included in this study group) who belong in this same category; patients who are referred for and expect surgery, who are apparently perfectly good surgical risks and yet, in my opinion, should not be operated upon. Given a robust man in the early sixties, active in the business or professional world, who has a moderate degree of prostatic enlargement, who has 2 ounces or a little more of clear residual urine, who voids once or twice at night and whose stream is sometimes a little slow in starting, such a man should not, in my opinion, be subjected to the risk (and there is always a risk) of any form of surgical operation, provided that: he is intelligent and is made thoroughly familiar with his condition and prospects, provided too that he is able and willing to comply with obvious hygienic regulations, including the careful avoidance of excesses, alcoholic, dietary and otherwise, provided also that neither his business

nor habits are such as to remove him for long periods of time from ready access to skilled surgical attention and finally provided that he will report at reasonable intervals for a check on his progress. The same course of reasoning applies under similar conditions to men in the middle eighties, perhaps retired from business, reasonably good operative risks, if operation were indicated and yet whose span of life expectancy is only two or three years at the best. This attitude may seem ultraconservative but I believe it is correct. I think that those of us who draw our patients from a comparatively small radius and are therefore able to keep in more intimate touch with them are prone to entertain a more conservative attitude than exists in a few of the larger clinics, many of whose patients come from great distances. I am quite sure that many patients are operated upon, and quite properly so, in some of the larger clinics who would be treated expectantly by some of us who do our work in smaller clinics. Most of these patients do not require nor are they benefited by any form of treatment other than the hygienic measures alluded to. There are, however, a few patients who are very definitely benefited by simple local measures. The man with a moderate degree of obstruction, clear urine and a large soft, boggy, elastic prostate may, not infrequently, be much improved and operation indefinitely deferred by simple massage. Please do not infer from this that I recommend or practice this policy as a routine procedure. I do maintain that in properly selected cases it is of definite value and this is based upon a sound pathological background. It is my understanding that the histological changes in the ordinary case of prostatic hypertrophy, the so-called adenomatous hyperplasia, begin as a fibrosis surrounding the prostatic ducts near their exit. These changes have usually been interpreted as inflammatory in nature. I am convinced from a series of studies conducted at our clinic, which consisted in careful sections of a large number of prostates removed at operation plus also a careful study of prostates removed at autopsy from patients of all ages dying from various cardiovascular lesions and which showed a striking similarity, that these evidences of early fibrosis are primarily vascular in origin. I have discussed this at some length in another paper.[1] At any rate fibrosis is followed by constriction of the ducts and gross overdistention of the prostatic acini, which constitutes the bulk of the enlargement in the early stages. This being the case: the histological picture being one of vascular deterioration, fibrosis, duct stricture, and acini overdistended with the products of secretion, it logically follows that improvement clinically and histologically should follow massage. I am sure that this is true in a small number of carefully selected cases. This histological conception provides also a rational background for the work which Caulk has been doing and his published results over a period of several years. He claims that following the removal of relatively small portions of the prostate at the bladder neck and floor of the deep urethra, the remainder of the gland atrophies or shrinks. Exactly the same conception may of course be applied to the newer methods of resection. However, I do not think that this part of the problem is by any means settled as yet.

And now that we have considered briefly that small group of cases that can be handled conservatively, let us proceed to a consideration of that much larger group of cases wherein the degree of obstruction and severity of symptoms demand some form of surgical relief. Here the choice of procedure will depend, or should depend, first and foremost upon the type of prostatic disease with which we are dealing and secondarily upon the physical vigor and operability of the individual. Without making an attempt to be too scientific or to express this thought with any degree of mathematical

accuracy, I think it is safe to say that the great majority of cases of prostatism will fall under the head of what may roughly be called general prostatic enlargement. I believe that the majority of these cases are best handled by means of the two-stage suprapubic operation. That I am sure is my own attitude and I see no present reason for changing it. In the present series of cases studied, out of 93 operations performed (excluding cystotomies only), 65 were of this type. I realize that there are a number of excellent operators who prefer and practice almost routinely the one-stage suprapubic operation, claiming the added advantage of better visualization, more accurate removal of all obstructing elements and more accurate control of hemorrhage. This is all true in a measure although I do not personally subscribe to some of the more or less complicated methods of suture of the bladder neck and prostatic bed following suprapubic prostatectomy. I think that these advantages, if they are advantages, are far more than balanced by the disadvantage of less adequate preliminary drainage and prolonged time of operation and I am sure that added time, even with block anesthesia, is a factor to some of these old men. There is very little difference in the length of hospitalization for the two groups, and right here I should like to make another point and I cannot stress my attitude on this point too vigorously. I do not think that the element of time should enter very largely if at all into our consideration when electing our choice of procedure. After all, what difference does a few weeks, a few more hospital days and a few extra dressings mean to our old patient if, by trying to cut corners, we add even one iota to the risk involved. I have no quarrel with the men who prefer to practice more or less routinely perineal prostatectomy. Their mortality statistics would appear to be a shade better and their end results probably just as good. One cannot be too extravagant in praise of the work done by Young in developing the technique of perineal prostatectomy and placing it upon a sound anatomical basis. There is only one comment which I would stress in comparing the two operations and that is the matter of general applicability. It would seem to me that all cases of the type under consideration are suitable for suprapubic attack while there are a few, including the huge intravesical growth, which I do not believe that even the most ardent perineal prostatectionist would consider approaching by this route.

I can best sum up my personal attitude toward these two operations by saying that if I had to have my own prostate removed and it were to be done in a clinic where perineal prostatectomy was more or less of a routine procedure, I should expect and hope that it would be done through the perineal route. On the other hand, if it were to be done in most of the clinics in this country, I should expect and *most ardently hope* that it would be done suprapubically. In my own small group there were one perineal prostatectomy and 5 one-stage suprapubic operations. It is my feeling that the great majority of cases, comprising this group which I have roughly classified as ordinary prostatic enlargement, are being handled, and properly so, by means of one form or another of formal prostatectomy. It is my feeling too that this attitude should and will persist for a long time, perhaps indefinitely and that other methods of treatment should be reserved for a smaller group of carefully selected cases. Time alone can tell how broad or narrow this group may be.

Let us now proceed to a consideration of the most recent and most dramatic contribution of transurethral operations. I think this has been one of the most important contributions to urology made in recent years and that men like Caulk, Stern, Davis, McCarthy, Alcock and others are entitled to no end of credit for the vast amount of work which they have done in developing and perfecting this

method. Yet on the other hand I frankly feel that they have been over-enthusiastic in their attitude and have stretched their indications beyond the limits of rational surgery. This attitude is perhaps commendable in a way for the time being since it is only by means of such enthusiasm that new ideas may be carried forward and their merit properly evaluated. However if this attitude is persisted in without an occasional soft pedal applied here and there, I believe it will actually do harm and retard progress. May I at this time interpolate one thought. The papers we read and the discussions which we contribute at these meetings accomplish two ends, one immediate, the other more remote. First we thresh out many mooted points and clarify many obscure situations among and for ourselves and out of our differences evolve that which spells progress. Secondly, our conclusions, sometimes a bit immature, are immediately adopted as a solemn text by hundreds of occasional operators whose results are never published and whose mortality statistics are buried with their patients. If for no other reason than that, it behooves us to be very conservative in our conclusions. I think that Alcock is doing a splendid piece of work. You are of course all familiar with it. He has for over a year now, with his great wealth of material, employed the electrotome to the exclusion of all other methods. He has approached the problem with an open mind and is doing his job with the avowed purpose of evaluating for himself and of course for urologists everywhere the merits and demerits of the procedure. You are referred to his paper for exact statistics. It is interesting to note that his mortality for his first 50 cases was excessively high, while that of his later cases was very low. This would seem to indicate that the mortality depended in large measure upon the degree of technical skill. It would also seem to indicate that, in the near future, many lives will be sacrificed upon the altar of urological education. All of us, of course, have our ear to the ground waiting for Alcock's end-results, as we have for the end results of Davis, McCarthy and others who are using this method extensively. In our own small series there were 12* cases of electrotome resections, with one death directly attributable to the operation. In this case there was intraperitoneal rupture of the bladder. The operation was done under spinal anesthesia, which according to McCarthy is contraindicated in these cases. Of course it is too early to venture any predictions as to our end-results. The immediate results appear satisfactory. The place which this new procedure will eventually occupy will depend very largely upon two factors, the operative risk and the end-result. As I said before I do not believe that the number of hospital days is entirely a valid factor. While the published reports of some of the pioneers might lead one to believe that the operative risk is a negligible factor, I have a feeling that when further returns are in, the average mortality may well be comparable with that of formal prostatectomy as now done in most of our clinics. We have already Alcock's high mortality in his early cases, my own death in a very small series and there have been a few others which have come to my attention (unofficially, so to speak), cases operated upon in small hospitals by "occasional" operators. These cases of course will never be published.

It is altogether too early to form any conclusions as to end-results. I could make this last statement without fear of contradiction except for one thing and that is the work of Caulk. While the technique of his operation differs somewhat from that of the newer methods, the operations are practically identical and he has been working long enough, followed his cases and published his results to

* At the present writing, November 1, 1932, 12 more cases have been operated upon by this method, with no mortality and no morbidity and with excellent primary results.

the end that his conclusions are of definite value and, we must admit, lend support to the attitude of some of the other enthusiasts. I do not know what to say to this other than that, perhaps, we need even more time and experience. My own attitude is that, in the light of our present knowledge and experience, the electrotome should be reserved for small median lobe hypertrophies and large thick hyperplastic median bars. This has been my practice, therefore the few cases in my own series were of that group.

For the fibrotic median bars and minor degrees of obstruction sometimes noted after prostatectomy and caused either by scar tissue or small nubbins of prostate which have been overlooked or have recurred, I much prefer the Caulk technique to any other form of procedure. The removal of a small amount only of tissue is required, two or three bites being normally ample. The apparatus is much less complicated, the technique is simple, the entire operation can be completed quickly, safely and positively and the results in my hands have been uniformly excellent. There were 6 of these operations in my group.

I have reserved for final consideration a group of cases which have until recently given me more trouble than any of the others. I refer to the small fibrotic prostate, sclerosis of the bladder neck if you like, associated with a high degree of obstruction and complicated, as they frequently are, by prostatic calculi. I have operated in a great many of these cases by various methods and have not until recent years had a single case in which I was entirely satisfied with my results. I was far from satisfied with the results of transurethral procedures and it had been my practice to approach most of my cases by means of a one-stage suprapubic operation for the purpose of securing good exposure, ease of approach and good visualization. I have toiled laboriously with my finger, my finger nail and various types of punch forceps and have had to show for my prolonged efforts a few insignificant bits of tissue, a little gravel and a ragged-looking bladder neck. I am sure that many of you will recall similar experiences. I have always felt, at the end of such an operation, that I had done a very unsatisfactory and a very unsurgical sort of a job and the later results have invariably warranted that attitude. My patients have reported later at the office or clinic with their residual urine markedly reduced but still present in fair amount, the character of their stream much improved but far from satisfactory and, most important of all, the dysuria and frequency much the same as before operation. In other words, an entirely unsatisfactory result.

I believe that the answer to this very trying problem consists in radical resection of the prostate and sclerosed bladder neck by the perineal route as recommended by Crabtree.

This operation is based upon sound surgical and anatomical principles and, in my judgment, Crabtree has made a contribution quite as important as the much-heralded transurethral resection. For some reason or reasons, however, this operation does not appear to have caught the imagination or engaged the attention of urologists in general and has not been accorded the consideration to which it is entitled. I believe there are two reasons for this attitude: first, the fear of technical difficulties and secondly, the dread of incontinence following operation. A large number of urologists, perhaps the majority, have had very little or no training in perineal surgery and they quite naturally contemplate a careful, accurate dissection of the perineum with a certain amount of fear and trembling. I can speak very feelingly on that subject since I formerly belonged in that group myself. (There was only one perineal prostatectomy in my present series.) This is however by no means an unsurmountable objection. I am sure that anyone with a fair degree of natural surgical skill, a careful review of

the anatomy, who has once seen the operation done, will have no special difficulties. That has been my experience and I consider myself only an average operator. In fact, strange as it may seem, I have found this operation much simpler from a technical point of view than the ordinary perineal prostatectomy. I shall make no effort at this time to describe the technique. That is amply covered in Crabtree's papers, with which you are all familiar.

And now on the second point: the fear of postoperative incontinence. I see no surgical or anatomical reason why, if the operation is properly performed, this complication should enter very largely into our consideration. While my own personal experience has been limited to 5 of these operations, and while I realize that such a small group means little or nothing from a statistical point of view, even so small a group is convincing to the individual operator. My results have been excellent, there has been no incontinence and only one operative complication. This occurred in a man of forty-four with a grossly infected prostate and a high degree of obstruction. He had been subjected, before coming under my care, to three or four punch operations with no improvement in his condition. He had a marked degree of periprostatitis, the perineal dissection was moderately difficult and in the course of this dissection an accidental wound was made in the rectum. This was repaired and the operation completed. His immediate convalescence was complicated by a breakdown in the rectal wound and a fecal fistula which finally closed spontaneously and at the present time, one year after operation, he has an absolutely perfect result.

Crabtree in a recent personal communication reports a total of 26 cases operated upon by this method over a period of eight years. (This, by the way, is fair evidence that he is selecting his cases carefully.) There was no mortality; there was one case of partial incontinence lasting three or four months and eventually going on to complete recovery; one case was "doubtful." All the others had perfect results with no incontinence and no residual urine.

Of course it will take a long time and the experience and results of many operators before the indications and merits of this operation can be finally determined. I am confident, however, that it will eventually occupy an important place.

In conclusion, I should like once more to stress the one point which I have attempted to make in this paper. Prostatism provides us with a wide variety of problems; we have available a wide variety of methods of treatment; and it devolves upon us to make every effort to elect the procedure which is best adapted to each individual case. I realize that my paper might be more convincing if it were bolstered with a mass of statistical evidence. It has not, however, been a statistical paper but rather a more or less philosophical contemplation of the whole problem, an expression of my personal views, for what they are worth upon a few of the mooted points and an effort to provide a suitable groundwork upon which to base what I trust may be a profitable discussion.

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SPONTANEOUS PERFORATION OF THE BLADDER

SECONDARY TO OSTEOMYELITIS OF THE PELVIS*

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THERE have been a number of case reports of spontaneous perforation of the bladder secondary to suppurative processes in adjacent structures. These include pyosalpinx, appendicular abscesses, diverticulitis and carcinoma of the colon and tuberculosis of the cecum and small bowel.

Reports of perforation from abscesses associated with osteomyelitis of the pelvis are rare. La Pena in 1931 was able to find only 5 and added one of his own. In a discussion of Chauvin's paper before the French Society of Urology in November, 1928, Maisonet mentions 2 cases, Marion one and Andre one. All except Andre's were observed during the war and were associated with injury to the pubic bone. This brings the total to 10 cases.

From observation of 4 cases of severe chronic osteomyelitis of the pelvis in children, either primary or secondary to suppurative arthritis of the hip, it is our belief that this complication is imminent in many instances in suppurative lesions of the pelvic bones. This statement is based on the finding in all 4 cases of a marked displacement of the bladder by the intrapelvic intrusion of an enormous involucrum and the perforation of the bladder in 2 by sequestra with the formation of osteovesical fistulae. It was assumed that perforation was impending in the other 2 cases because of the existence of the same engendering factors present in the two with perforation.

The displacement is caused by a massive involucrum and not by a pelvic abscess. In each of the 2 cases with perforation the sequestrum plugged the opening of the osteovesical fistula. In one, the opening was in the lateral aspect of the basal zone and in the other, in the fundal zone. In both, the side of the bladder involved was firmly adherent to the involucrum with a large amount of fungoid or granulomatous tissue between the bones and the bladder in some areas.

The perforation was chronic or subacute with the bladder wall firmly adherent to the involucrum, so that there was no extravasation, urinary leakage or any evidence that there had been.

In the 2 cases without perforation, there were no urinary signs or symptoms and in the 2 with perforation, attention was called to this complication simply because of a persistent pyuria. There were no subjective symptoms.

For this reason these cases are reported to call attention to the necessity of a routine examination of the urinary tract in all chronic suppurative lesions of the hip or pelvic bones, in children.

CASE REPORTS

CASE 1. J. G., a boy twelve years old, was admitted to the Children's Orthopedic Hospital in January, 1929, with osteomyelitis of the left femur and ilium, which had been caused by a fall three years before. He was emaciated and toxic and there were discharging sinuses from the upper third of the left thigh and from the region of the left sacroiliac joint and anterior superior spine of the ilium.

There were no urinary symptoms but the urine contained pus and streptococci on smear and culture. No tubercle bacilli were found and the von Pirquet and Mantoux reactions were negative. Kidney functional tests showed no renal insufficiency.

Roentgenograms (Fig. 1) showed an osteomyelitis of the left ilium with a suppurative

* Read before the Eighth Annual Meeting of the Western Branch Society of the American Urological Association, Portland, Oregon, July 2, 1932.

arthritis of the left hip. On cystography the bladder was found to be displaced upward and to the right (Fig. 2). A tentative diagnosis was made of spontaneous perforation of the bladder by an intrapelvic abscess secondary to the osteomyelitis. This apparently was confirmed by the cystoscopic examination at which time a large granuloma, which discharged thick pus, was seen in the left basal zone.

Fig 1. Case 1. Osteomyelitis of the left ilium. A, Sequestrum.

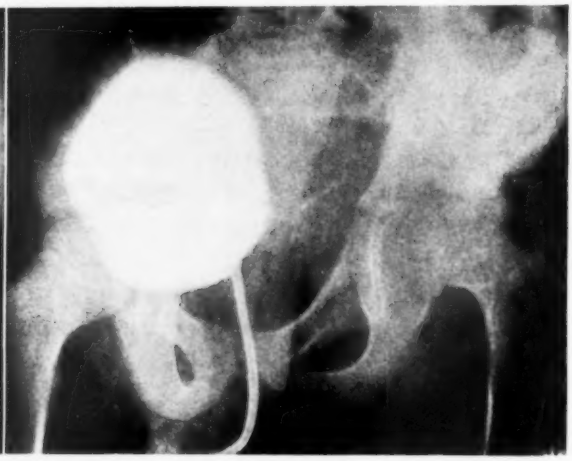

Fig. 2. Case 1. Cystogram showing displacement of bladder upward and to right by a large involucrum from osteomyelitis of the left ilium. Despite fact that bladder was perforated by a sequestrum there was no extravasation when bladder was distended by an opaque fluid. Process is a chronic or subacute perforation with bladder firmly adherent to involucrum before perforation takes place.

Operation: On February 16, 1929, the bladder was exposed extraperitoneally, through a left Gibson incision. No intrapelvic abscess was found but the entire lower half of the bladder was adherent to a large bony mass which filled the left half of the pelvis. The bladder was freed as far as possible down to the base. It was then opened and a sequestrum was found projecting through the fistulous opening indicated by the granuloma seen on cystoscopy. The sequestrum was removed, the bladder freed from the sinus and an area of infiltrated and degenerated bladder wall removed for 3 cm. around the perforation. The opening was closed in three layers from the outside and the bladder drained suprapubically. The hip was then drained and the sinuses injected with dichloramine T. The bladder wound healed rapidly and urination was established in three weeks.

Fig. 3. Case 11. Suppurative arthritis of left hip.

Fig. 4. Case 11. Roentgenograms demonstrating progression of infection with sequestra.

He later developed osteomyelitis of the left humerus, erysipelas and an abscess of the scalp.

Fig. 5. Case II. Cystogram showing filling defect and flattening of left vesical margin caused by massive involucrum from osteomyelitis of ilium. Despite fact that bladder was perforated by a sequestrum there was no extravasation on distending bladder with an opaque fluid. Sequestrum plugged opening.

Fig. 6. Case II. Roentgenograms taken four months after operation. No sequestra are present. There is an ankylosis of left hip joint.

A follow-up note was made in January, 1932, three years after the onset: "Patient's condition, good; one pound overweight, active, no complaints, slight limp, no open sinuses. There is limitation of both internal and external rotation of left leg and marked limitation of abduction, less of adduction. He has almost full flexion and extension. No urinary complaints, urine normal. To report in one year."

pain in his left groin. He was treated for inguinal lymphadenitis, but in a few weeks was unable to walk. One week prior to admission a spica cast was applied to the left hip. *X*-ray pictures showed a suppurative arthritis of the left hip (Fig. 3).

After traction and immobilization for four months, he was discharged with a spica walking cast and readmitted two months later. An *x*-ray picture at that time (Fig. 4) showed a progression of the infection with sequestra in the pelvis. In addition there was a swelling in the left inguinal region which drained thick pus. He was placed on a Bradford frame with Buck's extension for eight months during which time

Fig. 7. Case III. Roentgenogram showing osteomyelitis of right ischium.

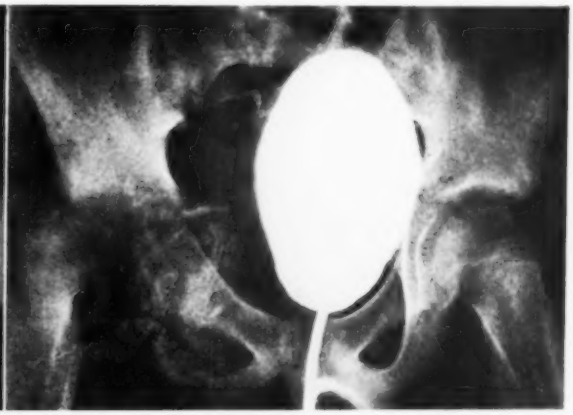

Fig. 8. Case III. Cystogram showing displacement of bladder to left. There was no perforation in this case.

Case II. M. D., a boy ten years old, was admitted to the Children's Orthopedic Hospital in June, 1930, with a diagnosis of suppurative arthritis of the left hip. Four months before he had had a severe cold followed by he had numerous blood transfusions. On August 19, 1931, his urine, which had previously been essentially normal, became cloudy and on analysis showed a heavy cloud of albumin,

many pus cells and a few gram negative rods and staphylococci. These urinary changes were associated with no subjective symptoms. The von Pirquet and Mantoux tests and guinea pig inoculations were negative for tuberculosis. Renal function tests were within normal limits. A cystogram (Fig. 5) showed a filling defect and flattening of the left lateral vesical margin. On intravenous urography there was no evidence of upper tract disease but the filling defect in the bladder was evident.

Fig. 9. Case III. Roentgenogram showing progression of bony destruction. Note sequestra in pelvic cavity. No evidence of perforation when this patient was last examined.

On cystoscopic examination the bladder mucosa was normal except for a fibrinopurulent exudate in the basal zone and a granuloma in the left fundal zone. The ureteral orifices were normal in position and appearance.

From our experience with the former case we were able to make a diagnosis of spontaneous perforation of the bladder secondary to osteomyelitis of the ileum.

Fig. 10. Case IV. Roentgenogram showing advanced osteomyelitis of left ilium.

Operation: On October 1, 1931, the bladder was exposed extraperitoneally through a midline incision. The left lateral wall was firmly fixed to a mass of new bone in the left pelvis. It was freed down to a fistulous opening which contained a sequestrum that had perforated the bladder. The margins of the fistula were excised and the opening closed. Three large sequestra were removed from a cavity filled with granulation tissue, just outside the bladder. The hip and pelvic cavity were

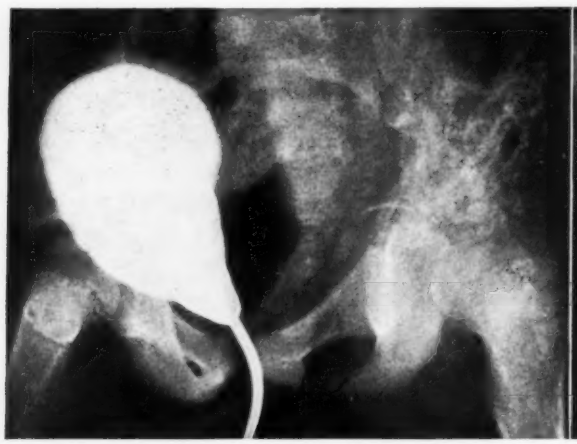

Fig. 11. Case IV. Cystogram showing displacement of bladder to right.

Fig. 12. Case IV. Roentgenogram showing almost complete destruction of left ilium. Despite marked bladder displacement and numerous sequestra there was no evidence of perforation one year after onset of this condition.

drained and the bladder closed with drainage. The patient was discharged four months later with an ankylosis of the left hip (Fig. 6). The urine was essentially normal except for a positive culture of staphylococci.

We are reporting, briefly, 2 other cases of a similar nature except for the perforation, to demonstrate that this displacement of the bladder from the intrapelvic intrusion of a mass of new bone, fungoid and granulomatous tissue, must be fairly constant in suppurative lesions of the pelvic bones and that because of it, perforation is a complication to be anticipated.

Case III. J. W., a boy eleven years old, was admitted to the Children's Orthopedic Hospital, August, 1931, complaining of pain in the right hip and inability to walk. *X*-ray pictures (Fig. 7) showed an osteomyelitis of the right ischium. He was placed on a Bradford frame with traction and one month after admission the right hip was drained.

There were no urinary symptoms and except for an occasional pus cell, the urine was normal. However, a cystogram (Fig. 8) showed displacement of the bladder to the left, undoubtedly by a condition similar to that demonstrated in the two previous cases. Another picture (Fig. 9) taken in January showed a progression of the bony destruction and sequestra in the pelvis. There was no evidence of perforation up until April 1, when this patient was last examined.

Case IV. The fourth patient was a girl, ten years old, admitted to the Children's Orthopedic Hospital July, 1931, with fever, nausea and vomiting and tenderness over the region of the left hip, of one week's duration.

An osteomyelitis of the ilium was drained the day after admission. The condition was progressive and there was a good deal of bony destruction in the left ilium after one month (Fig. 10). A cystogram was made which showed a marked displacement of the bladder to the right (Fig. 11). A cystoscopic examination was not done because of her critical condition. Another *x*-ray picture taken five months after the onset showed almost complete destruction of the left ilium (Fig. 12). However, the urine was normal. No perforation was evident on cystoscopic examination one month ago.

SUMMARY

No mention of the condition just described can be found in a review of the literature. A few cases of perforation of the bladder by sequestra from nontuberculous osteomyelitis have been reported but the displacement of the bladder by a massive involucrum as a constantly associated condition has not been considered. We feel that it is fairly frequent from the fact that it was present in each of the 4 cases of osteomyelitis of the pelvis we have had the opportunity to examine.

The absence of signs and symptoms referable to the urinary tract accounts for the failure to consider this possible urinary complication. Even in the 2 cases with perforation there were no subjective symptoms and examination was undertaken because of persistent pyuria.

The clinical significance of the condition lies of course in the possibility of perforation of the bladder, which occurred in 2 cases and which might be assumed to be impending in the others, where the engendering factors were the same.

This should be an additional reason for early and thorough drainage of all suppurative processes in the hip joint or pelvic bones.

The operation for the osteovesical fistula is at times difficult because of the firm adhesions of the contiguous portion of the bladder to the involucrum and the infiltration about the fistula with danger of laceration. Healing is rapid and the operative results are good. Once corrected the condition does not tend to recur provided adequate drainage of the osteomyelitis is established.

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ANOMALIES OF THE LUMBOSACRAL SPINE*

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THE purpose of this paper is twofold: first, to give a brief résumé of the more recent publications on this subject, and second, to add to the literature the record of a most unusual and extremely interesting case.

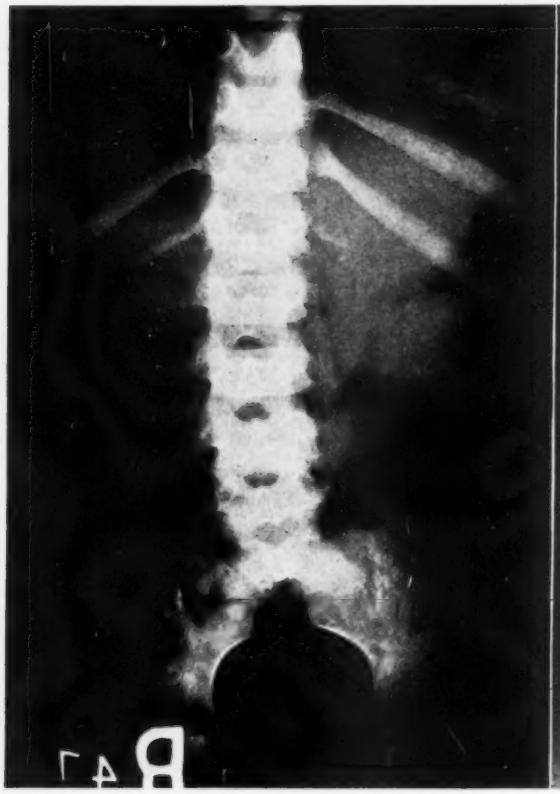

FIG. 1. Absence of sacrum and coccyx.

FIG. 2. Six lumbar vertebrae.

Anomalies of the vertebral column, particularly of the lumbosacral region, are of such common occurrence that one may well hesitate in making a definition of what constitutes a normal spine. These various anomalies will be discussed according to the following outline:

I. Numerical variations in the vertebrae
II. Abnormalities of the vertebrae, morphologically
   A. Transverse processes
      1. Lumbar ribs
      2. Impingement
   B. Laminae
      1. Spina bifida occulta and vera
      2. Isthmus—pars interarticularis
   C. Bodies
III. Horizontal sacrum
IV. Case of apparent double lumbosacral spine

I. NUMERICAL VARIATIONS

Many anatomical specimens and roentgenograms show variations in the number of segments present in the lumbosacral spine and in the sacrum and coccyx.

* Presented before the King County Medical Society, Seattle, Sept. 19, 1932.

Fitch, quoted by Sutherland, in 1909 reported the case of a child in which the sacrum and coccyx were completely absent. This also holds true in the lumbodorsal region. With the evolutionary development of man, there goes a tendency toward

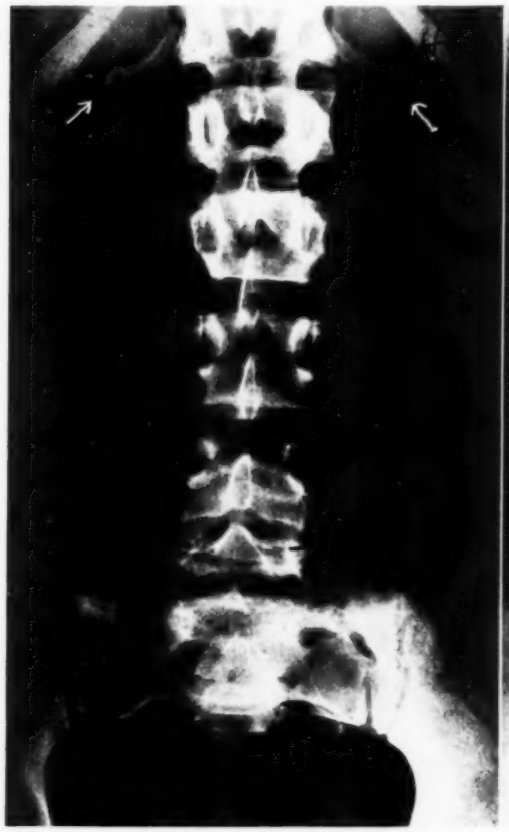

Fig. 3. Lumbar ribs.

Fig. 4. Fractures of transverse processes.

Figure 1, the radiograph of a patient at the Children's Orthopedic Hospital, is an illustration of this type of spinal anomaly, the sacrum and coccyx being almost entirely absent. Crookshank, quoted by the same author, in 1914 reported a case in which there was no lumbar spine. The pelvis in this case was imperfect. Sutherland, in 1922, reported 2 cases, one showing an absence of the lower two sacral segments, the other a rudimentary sacrum on one side.

Bardeen states that 16 per cent of all vertebral columns show numerical variations in the segments present. There may be no actual variation in the total number of segments, but sacralization of the last lumbar vertebra or lumbarization of the first sacral segment, frequently occurs. shortening of the spinal column. Sir Arthur Keith states that in lower primates, the twenty-seventh vertebra forms the first sacral segment; in man it is usually the twenty-fifth. In a study of 141 skeletons, Willis finds that in 5.6 per cent of cases there is an actual variation in the number of presacral segments. (Fig. 2.)

The effect of these anomalies, if there be an actual variation in the number of segments, can hardly be more than a mere decrease or increase in the length of the trunk.

II. Abnormalities of the Vertebrae

A. *Transverse Processes*

1. *Lumbar Ribs.* Abnormalities of the transverse processes of the lumbar verte-

brae are of not infrequent occurrence. Camurati, in a study of 500 roentgenograms, reports lumbar ribs in 1.22 per cent of cases (Fig. 3). This is of considerable medicolegal importance in that rudimentary ribs may stimulate very closely fractures of the transverse processes. A fracture, however, will usually show an irregular fracture line when seen in the radiograph, whereas a lumbar rib will have a smooth line of articulation (Fig. 4). Clinically, the fractures will give rise to definite areas of local tenderness. The lumbar ribs may cause vasomotor and sensory disturbances.

2. *Impingement.* The transverse processes of the last lumbar vertebra may be so enlarged as to impinge upon the ilium or sacrum (Fig. 5). Its occurrence without contact with the sacrum is unusual. It was found in but 0.54 per cent of the spinal columns examined by Willis. Hiese reports sacralization in 4.19 per cent of cases in his studies. Its occurrence is part of the process of shortening which is going on in the vertebral column of man. Its presence, however, may give rise to the formation of bursae or areas of pressure, with clinical manifestations such as pain or deviation of the spine to one side. A case is here presented which illustrates the point.

Fig. 5. Impingement of fifth transverse process on sacrum; entirely asymptomatic in this type.

Fig. 6. Impingement of fifth transverse process, producing symptoms.

Mrs. Z., aged forty-two, with the complaint of pain in the low back since the age of eighteen years. The pain was definitely localized on the left side, just above the sacrum. *X*-rays showed an impinging transverse process with definite bone condensation at the site of contact. Gynecological and medical consultation brought out the fact that the patient was in need of a perineal repair, and that she was badly constipated. These difficulties were attended to, but the patient experienced no relief from the pain in her back. In view of the *x*-ray findings (Fig. 6), it was decided that the process should be removed. This was therefore done. At operation, an articulation was found between the fifth transverse process and the sacrum. It was covered with very smooth,

white, fibrous tissue. The process and the articulation with the sacrum were removed. The specimen is shown in Figure 7. Convalescence was uneventful except for some pain along the course of the sciatic nerve, persisting for a few weeks. *X*-ray showed that the process had been completely removed (Fig. 8). A month after the operation the patient was entirely free of her old back pain. Since that time she has continued to remain entirely free of pain.

Fig. 7. Specimen removed at operation.

Fig. 8. Radiograph taken after operation. Impinging process completely removed.

B. *Laminae*

1. *Spina Bifida.* Spina bifida may be entirely concealed beneath the integument, the spina bifida occulta (Fig. 9), or it may be manifest, the spina bifida vera (Fig. 10). Both are due to a failure of fusion of the two lateral halves of the neural arches. Fusion in the sacral region does not occur before the age of seven years, and roentgenologic evidences of failure of fusion before this age cannot be interpreted as abnormal. Wheeler, in a study of 1000 radiographs of male adults, found incomplete closure of the posterior arch of the fifth lumbar vertebra in 1.2 per cent of cases. Willis reports clefts in the posterior arches of the fifth lumbar vertebra in 1.2 per cent of 1471 specimens studies. Varying percentages are reported by numerous writers.

The presence of a spina bifida gives rise to cord symptoms in a high percentage of cases. Incontinence and enuresis are common. There is often paralysis of weakness of the lower extremities. This paralysis may be either spastic or flaccid in character. Trophic ulcers occur frequently and there may be anesthesia or hyperesthesia, often of the saddle type. Deformities may develop as the patient grows older, the most common being the claw foot. Frequently there is an equinus or a varus deformity of the feet. Spina bifida occulta is a frequent cause of low back pain. In a study of 100 cases of low back pain, Willis was able to demonstrate clefts in 10 per cent.

In spina bifida vera or manifesta there exists an actual herniation of the coverings of the cord. The symptoms and findings are similar to those present in the milder involvement of spina bifida occulta, but they are more severe and extensive in character.

2. *Lesions of the Isthmus.* Abnormalities may occur in the neural arches between the superior and inferior articular processes (Fig. 11). Willis, in 1923, in an examination of 748 spines, found separation of the neural arch in 4.28 per cent of cases. In a study of 1520 vertebral columns in the Hamann Museum he found defects of one or both laminae in 79 instances. Congdon, in a recent publication, reports the presence of lesions of the isthmus in

5 per cent of the 200 specimens that he collected from the old Indian burial grounds at Wenatchee (Figs. 12 and 13).

Fig. 9. Spina bifida occulta.

Fig. 10. Spina bifida vera.

Neugebauer attributes these defects to incomplete ossification of the pars interarticularis. When this defect occurs the body of the affected vertebra loses its bony connection with the inferior articular processes. As a result, spondylolisthesis may occur, the body of the affected vertebra slipping forward, carrying with it the superimposed spine (Fig. 14). Spondylolisthesis may also be caused by defects in the articulations. It may occur in any of the lumbar segments but the usual location is between the fifth lumbar vertebra and the sacrum. The basis of the lesion is undoubtedly congenital, although in many cases there is a history of trauma. All but one of the 1050 cases studied by Heise gave a history of trauma. Kleinberg feels that the dislocation is traumatic in origin in a large percentage of cases. In most instances, however, careful questioning will bring out the fact that the back has never been entirely normal. Trauma undoubtedly plays an important part in bringing about a change in a part that is congenitally defective. This slipping forward of one of the lumbar vertebrae usually gives rise to distressing symptoms. The onset is often sudden, following some injury. Backache is complained of in 95 per cent of cases. The pain is aggravated by strain or exercise. The lumbar spine appears shortened and there is a hollow or step at the lumbosacral junction. The back shows a deep and sharply kinked lordosis. Tenderness is present at the lumbosacral junction. The erector spinae group of muscles are in a state of spasm and are markedly tender. After a time the patient, in adjusting his body carriage to the position of the lumbar spine, begins to walk with a slow, waddling gait. The backache is persistent and disabling.

c. *Anomalies of Vertebral Bodies*

Platyspondyly. Congenital flattening of one or more of the vertebral bodies is of rare occurrence and its presence is confined almost entirely to the dorsal spine. Nearly

all cases originate in childhood as a result of rachitic involvement of the skeletal system, and are not truly congenital in its accompanying symptoms. Deformity and low back pain always form the basis of the patients' complaint.

Fig. 11. Lesion of isthmus.

origin. The condition requires differentiation from traumatic platyspondyly.

Synostosis. Congenital fusion of one or more of the lumbar vertebrae may occur (Fig. 15). Such cases have been reported by Boehm and Drehman, quoted by Steindler. Peabody reports a case in which the third and fourth lumbar segments are fused. The figure shown is that of a case at the Children's Orthopedic Hospital.

Hemivertebra. (Fig. 16.) Wedge-shaped vertebrae and parts of vertebrae are of not uncommon occurrence. The presence of the abnormal segments alters the contour of the spine, producing scoliosis with

Fig. 12. Separate neural arch (right) with normal vertebra (left). Specimens found in Indian burial grounds. (Courtesy of Dr. Congdon.)

III. HORIZONTAL SACRUM (FIG. 17)

In the normal pelvis, the anterior margin of the first lumbar vertebra forms with the anterior surface of the sacrum, an angle of about 42 degrees. With an increase in the horizontal position of the sacrum and in the normal lumbar lordosis, the tendency

Fig. 13. Lesion of isthmus and spondylolisthesis. From Indian burial grounds. (Courtesy of Dr. Congdon.)

is toward widening of the anterior portions of the intervertebral spaces between the lumbar segments. This is accompanied by a strained condition of the vertebral ligaments. Deep palpation in the midline of the abdomen will reveal tenderness over the anterior surface of the vertebral column. The more horizontal position of the sacrum also throws additional stress

FIG. 14. Spondylolisthesis.

FIG. 15. Congenital synostosis of second, third and fourth lumbar vertebrae.

FIG. 16. Hemivertebra. (Courtesy of Dr. Milgram.)

FIG. 17. Horizontal sacrum.

on the already unstable articulations, contributing further to the state of chronic ligamentous strain that develops. The

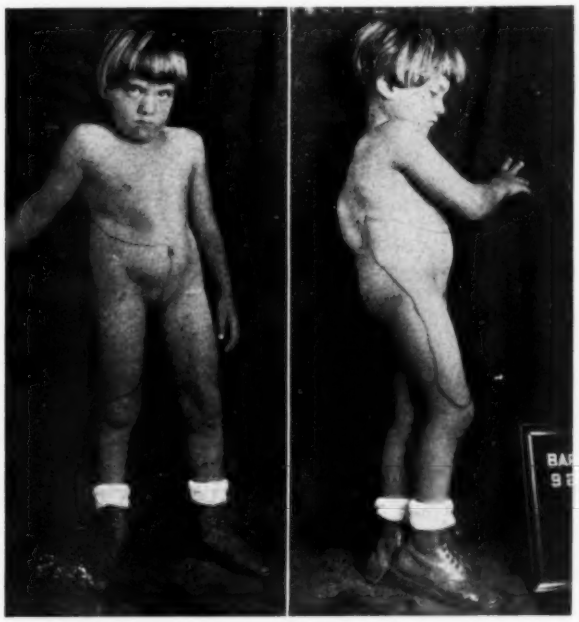

Fig. 18. Fig. 19.

Figs. 18 and 19. Double spine, showing area of anesthesia.

increased forward and downward thrust of the lumbar spine upon the upper portion of the sacrum may give rise to disturbances in the sacroiliac joints. The chief complaint of patients suffering from this lesion is persistent backache of a greater or lesser degree of severity.

IV. APPARENT DOUBLE LUMBOSACRAL SPINE

An unusual case representing an apparent double lumbosacral spine is here presented.

The patient, a female, six years of age, was brought to the Outpatient Department of the Children's Orthopedic Hospital on August 25, 1931, because of a slight limp and because of a large swelling over the low back. This mass had been present since birth. She was in good general health. On examination, the child was found in good general condition. The physical examination and laboratory work were essentially negative, except for the findings noted below. She walked with a limp on the right side. The adductors of the thighs were markedly contracted and there was present one inch of actual shortening on the right side. There was over an inch of atrophy of the right

Fig. 20. Double spine, anteroposterior view.

Fig. 21. Double spine, lateral view.

side. On the right side there was a questionable Babinski reaction. From the umbilicus to the knee, on the right side, there was present an

area of anesthesia, corresponding to the sensory distribution of the eleventh and twelfth dorsal, and the first, second and third lumbar segments. (Figs. 18 and 19.) In the lower dorsal and the lumbar region, there was present a large, soft swelling, entirely covered by skin, in which numerous bony projections could be palpated. Radiographs (Figs. 20 and 21), revealed the fact that from the seventh dorsal vertebra down to and including the sacrum, the vertebral column was apparently present in duplicate. Four rows of transverse processes and two distinct and separate sacra could be made out. In the lateral view, two definite coccyges and sacra were evident.

The writer has been unable to find in the literature any record of any case showing a spinal anomaly of similar character. The child was in good health and apparently normal, except for the disturbances noted. It was thought to be hazardous and almost impossible to study the case further by means of opaque media. Therefore the assumption of a double lumbosacral spine must rest on radiographic evidence.

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PREPARATION OF DEXTROSE AND SALINE SOLUTIONS AND APPARATUS FOR INTRAVENOUS AND SUBCUTANEOUS USE

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NOTE

During the last few years there have been more reactions than seemed justified following the intravenous or subcutaneous administration of glucose or saline on the surgical service of the Fifth Avenue Hospital. A committee of three members of the surgical department was appointed by me to investigate this problem. The committee found that there was no single article in the literature which considered all of the possible sources of trouble from the time the water was drawn from the tap until it was injected into the veins of the patient. It spent a great deal of time investigating this problem, and it seemed therefore advisable to publish its findings. The criticism may well arise that this report is extremely didactic, but if one considers that it is the report of a committee to a surgical service and that its recommendations are concretely given in order that the surgical department of the Fifth Avenue Hospital might describe in detail the technique I believe this criticism can be mitigated.

I wish to express my thanks to the committee for the enormous amount of time, thought and attention to detail it has expended in preparing this data.

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IN spite of the widespread use of intravenous and hypodermic infusions, there is no universal standard for the proper preparation of these solutions or the apparatus used in their administration.

The administration of infusions is occasionally followed by severe reactions.

It is the intention of this article to take up the causes and elimination of reactions following infusions, to describe a method of properly preparing glucose and saline solutions and the apparatus used in their administration.

CAUSES OF REACTIONS

Among the many theories advanced as to the causes of reactions are: the use of contaminated or improperly distilled water, the use of new rubber tubing, impure glucose, absorption of impurities from glassware, absorption of metals from the still, the temperature of the solution, the hydrogen-ion concentration of the solution, improper sterilization, presence of foreign bodies such as particles of glass and the speed of the injection.

A. *Contaminated Distilled Water:* It was demonstrated several years ago that about 50 per cent of all ordinary distilled water contained a fever-producing substance which was called pyrogen. This test was made from samples of water from several large cities: Boston, Chicago, Philadelphia.

Pyrogen is a product of bacterial origin: it is soluble and filterable and resistant to heat. Pyrogen depends upon the presence of a specific strain of bacteria described by Jordan as group X and XI of river water bacteria. Although these bacteria are removed by filtration, sterilization and ordinary distillation, the bacteria by-products are not removed. The presence of large numbers of other bacteria in water is not sufficient to produce pyrogen or render the water pyrogenic.

Pyrogen is a product of this one special group of bacteria and is a nitrogenous substance. It readily passes over with the distillate in an ordinary still unless a water spray trap is employed. The use of this water spray trap in the still is the only effectual method of eliminating pyrogen, as it is not removed by repeated ordinary

distillation, or by sterilization and will pass through a Berkefeld filter. This point cannot be emphasized too much, or too frequently, as it has been repeatedly shown that pyrogen is the greatest and most constant single factor in the cause of reactions.

Water containing pyrogen is referred to in the current literature as contaminated water and repeated distillation and sterilization in the ordinary manner will not remove the contamination. Contaminated water, having been properly distilled, immediately sterilized and preserved sterile will remain free from pyrogen.

Febrile reactions from pyrogenic water are less marked when the water solution is used subcutaneously or intraperitoneally than when used intravenously.

Since pyrogen may be developed in water in a comparatively short time, four days at the most, it is important that all solutions be made from freshly distilled and sterilized water.

Let me again emphasize that a single proper distillation will be non-pyrogenic while repeated ordinary distillation may be pyrogenic.

B. *Hydrogen-ion Concentration:* In a series of 55 infusions it was found that salines of alkaline p^H were more prone to give reactions. Normally distilled water is slightly on the acid side. The nearer the original p^H approached the alkaline side, the more frequent the reactions. That p^H in itself is not a causal factor was proved by buffering a solution of high p^H to a low p^H only to still have reactions occurring. The addition of ammonia to solutions of low p^H caused no reactions although the final p^H was over 8. The presence of alkaline impurities in the distilled water was shown to be the cause of reactions and upon investigation, the alkaline impurities were found to be due to the by-products of a special strain of bacteria or pyrogen. Once again, we find the importance of eliminating pyrogen from the distilled water.

C. *Impure Drugs:* Chemically impure glucose and sodium chloride may give reactions but the reactions do not consistently occur.

D. *Rubber Tubing:* This is also only a casual factor in the production of reactions. It has been shown that giving non-pyrogenic solutions through fresh rubber tubing and boiling non-pyrogenic solutions with fresh rubber corks so that the final solution smelled strongly of rubber, produced no reaction.

E. *Impurities from Glassware:* When a soft glass is used in the still, or to collect the distilled water or to contain the final solutions, it will occasionally impart an alkaline impurity to the solution.

F. *Impurities from Metals:* Faulty distillation in certain copper, nickel and zinc condensers will dissolve these metals. Tin, however, will not be dissolved.

G. *Temperature of the Solution:* The heat of the solution is also another variable factor in the cause of reactions.

Non-pyrogenic solutions were given at 20°C. and at 42°C. without producing reactions. When too hot, the patient complains of burning at the site of injection, but no reaction. Administration of cool solutions to patients with high temperature has seemingly caused a drop in body temperature without reaction or chill. Pyrogenic solutions given at any temperature will result in reactions. Solutions above 37°C. usually raise the blood pressure while solutions below 37°C. usually lower blood pressure.

H. *Improper Sterilization:* Repeated sterilization of glucose solutions under high pressure will cause a caramelization which sometimes results in severe reactions. A caramelized solution has a pale yellow to golden brown color and all such solutions should be discarded.

I. *Foreign Bodies in the Solution:* If a cotton or gauze plug is used in the mouth of the flask, some particles may become detached and drop into the solution.

In a series of experiments using ordinary ampoules of glucose and saline solutions

and opening these ampoules by means of filing and breaking, it was found that each of 100 ampoules contained numerous small particles of glass. The smallest number of particles contained in any ampoule was 200, and the largest number was over 500. In most instances these particles came from the inner side of the ampoule but in one instance it was demonstrated that some of the particles of glass came from the outside of the ampoule. These particles were usually small enough to pass easily through a 20 gauge needle.

J. *Rate of Injection:* There is no uniformity or standard as to what constitutes a slow or fast rate of injection. A slow rate of injection described by many authors varies from 2 to 4 c.c. per minute to 40 to 60 c.c. per minute.

Recent investigators have demonstrated that severe reactions called "speed shock" follow a very "rapid injection" of a solution intravenously. In these experiments, there was no measure of what constituted a "very rapid injection," other than that the syringe was emptied as fast as possible.

K. *Use of Low Grade Filter Papers:* The paper may contain starch bodies or loose fibers which may go into the solution.

L. *Individual Susceptibility to Glucose.*

ELIMINATION OF REACTIONS

A. & B. Since contaminated distilled water or pyrogenic water is the most constant cause of reactions, this is easily eliminated by the use of a still having a water or spray trap. Only freshly distilled water should be used in making up solutions which are immediately sterilized and preserved sterile by being sealed.

The test used for determining the presence of pyrogen is a delicate color test and depends upon the oxidation of potassium permanganate by boiling. Normally if distilled water is free of oxidizable substance, and thereby free of pyrogen, on boiling in this test it should retain its color for ten minutes.

The test is as follows:

Heat 100 c.c. of distilled water in a clean pyrex beaker to boiling, then acidulate with 10 c.c. of dilute sulphuric acid (10 per cent) and add 0.1 c.c. of twentieth normal potassium permanganate solution. The color of the solution should not be destroyed by continuing the boiling for ten minutes.

In applying this test to our samples of distilled water we frequently receive a positive result, so we had our engineer make and install a spray catcher in the still. This spray catcher is simply a baffle plate against which the column of stream strikes and is diverted to another direction, leaving any small drops of spray, which might otherwise pass over into the distillate, upon the under side of the plate. If the steam outlet to the condenser is sufficiently high so that by force of gravity the drops of spray cannot pass over, the same effect is accomplished.

Following the installation of this spray catcher our samples of distilled water have been repeatedly negative in the test for pyrogen.

C. With the establishment of dextrose standards as distinguished from glucose in the tenth revision of the U.S.P. any dextrose made by a reliable firm and conforming to the U.S.P. standards is acceptable for use. Other forms of dextrose and glucose may not be chemically pure and should not be used. The sodium chloride should likewise be chemically pure. It is important that only chemically pure drugs be used.

D. The rubber tubing employed should be made of pure gum rubber. When new red rubber tubing is used, due to sulphur content of free talc it should first be washed in soap and water, then rinsed in running water, then distilled water, then soaked in a solution of 4 per cent sodium hydroxide for one hour, then washed thoroughly and soaked in distilled water before being sterilized. No tap water should be used after the original washing as it contains gelatinous impurities which may adhere to the inner surface of the tubing.

E. Only hard or non-soluble glassware such as yena or pyrex should be used.

F. The still should be of glass or lined and soldered with block tin.

G. The solutions at the time of use should be about or slightly above body temperature.

The difference in the temperature of the solution in the container and the solution at the needle point will vary from 15 to 30 degrees, depending upon the length of rubber tubing and the rate of injection.

The solution in the container should be approximately 120°F. and the container should be surrounded by hot water bottles or other suitable apparatus to maintain this temperature.

H. Glucose solutions properly prepared and filtered at least five times through French filter paper are autoclaved without a vacuum for forty minutes at 5 pounds pressure. A higher pressure may cause the solution to become caramelized. Saline solutions are to be autoclaved for twenty minutes at 15 pound pressure.

I. Cotton or gauze plugs should not be used in the mounts of the flasks unless the flask part of the plug is covered with unlacquered cellophane paper.

When glass ampoules are used, a short time should elapse after the ampoule is opened to allow the particles of glass to settle to the bottom. The solution is then withdrawn, leaving a thin layer of the solution which contains the glass particles.

J. The rate of injection depends upon the concentration of the solution. A 25 per cent solution of glucose should be injected much slower than a 5 per cent solution. No solution should be injected at a rate greater than 5 to 10 c.c. per minute.

Recent work has shown that the therapeutic dose of glucose for the average sized individual is 75 gm.

This can be administered in any concentration of solution desired. Where there is a need of fluid as well as nutrition, an isotonic solution is preferable. Where a larger amount of fluid would embarrass the cardiovascular system, a hypertonic solution is to be used. It has been estimated that 90 to 100 minutes are required for the administration of a therapeutic dose of glucose regardless of the concentration of the solution used.

K. Only high grade filter paper should be used. Whatman number five is satisfactory.

L. Fortunately the incidence of individual susceptibility to glucose is rare. We do not know of any practical method of eliminating this cause of reaction.

OBSERVATIONS ON A SERIES OF INFUSIONS

In a series of 300 infusions, the temperature, pulse and respiration were recorded immediately before, immediately after and at one hour intervals for four hours following each infusion.

The thought behind these experiments was to find out if reactions, subclinical in degree, and unnoticed by the patients were occurring as manifested by a change in the temperature, pulse and respiration.

A standardized technique for the preparation and administration of the solutions was used throughout with the exception of the rate of the injection. The rate of injection, although varying in each infusion, was always within the safety margin.

Three clinical reactions, non-fatal, occurred in this series. The reactions were characterized by chills and elevation of the temperature 2 to 5 degrees, during or immediately following the infusions.

No clinical reactions occurred in afebrile patients. We were unable to determine the cause of these clinical reactions.

It was decided that a change in the temperature of as much as ½ degree would be classified as a sub-clinical reaction. There were a number of instances in which the temperature rose ½ or more degrees, but these occurred in postoperative patients or in those who had an abnormal elevation of the temperature at the time of the infusion, so that we were unable to determine definitely that the elevated temperature was due solely to the infusion. These

cases could therefore not be counted as infusion reactions.

There were a number of patients, about 60 per cent, both febrile and afebrile, who had no change or a decrease in the temperature following the infusion.

In studying the charts, we found that at times the temperature would be decreased or elevated as much as ½ degree and one hour later, it would be the reverse. In classifying these changes, if the primary change was as much as ½ degree and the secondary change could be accounted for by the patient's pathological condition, or if the secondary change was no greater than the primary, it was classified as to the primary change.

It is our belief that where no cause for temperature elevation exists prior to the infusion, the tendency is for the temperature to show no change or to be slightly lowered following the infusion. This occurred in 60 per cent of these observations.

As a rule the pulse and respirations followed the temperature elevation in approximately the usual relation.

The following is a suggested Technique for Preparation of Intravenous Solutions and Containers of Glucose, Normal Saline, 2 per cent Saline and Triple Distilled Water.

I. The containers are Erlenmeyer flasks made of non-soluble glass, such as yena, pyrex or kavalier. When received new, they are washed as follows:

1. Dusted out.
2. Rinsed with a 1 to 2 per cent solution of hydrochloric acid, U.S.P.
3. Washed in hot water.
4. Solution of washing soda (5 per cent).
5. Surgical soap solution, standard.
6. Rinsed with tap water.
7. Rinsed with fresh triple distilled water.

II. Flasks returned after the contents have been used are to be washed with:

1. Sulphuric bichromate cleaning solution (a technically concentrated sulphuric acid with sodium bichromate added).
2. Rinsed four times with tap water.
3. Rinsed two times with triple distilled water and dried.

If these flasks are to be set aside *after drying*, their mouths are to be covered with unlacquered cellophane paper tied on, until flasks are used. They should be sterilized to avoid development of moulds.

III. The fresh triple distilled water used for making up solutions for intravenous use and rinsing flasks shall be water distilled in a still of adequate capacity which cannot impart any foreign substance, either chemical or otherwise, to the distillate which can be detected by chemical or microscopic examination or which will give an undesired reaction in the human body when used intravenously.

The still should be lined with glass or lined and soldered with block tin and should contain a water spray trap. The distillate from the first still shall be distilled a second time and a third time. The time elapsing between the first, second and third distillation must be no more than two hours. The distillate shall not pass through or touch any rubber from the time it leaves the fluid in the first still until finally collected in the non-soluble glass Erlenmeyer flasks. Any conveyance necessary is to be done in clear glass tubing of non-soluble glass or block tin which is to be washed and rinsed with distilled water before the preparation of distilled water for intravenous solutions. Following the last distillation this water is to be immediately used for the preparation of solutions.

The vessels used for collecting distilled water are to be non-soluble glass Erlenmeyer flasks carefully washed and rinsed with triple distilled water. After being washed and rinsed, the flasks are to be dried by inverting on a wooden rack which supports the flasks on the outside and not by any projection inside the flask.

The term "fresh triple distilled water" indicates that not longer than two hours shall elapse after the third distillation and that it is to be kept during this time in the original collecting flasks, with tops covered with sterile metal tops or unlacquered cellophane.

IV. The solution of glucose (50 per cent) is to be made up in volumes of 50 c.c. and 100 c.c. per flask so that when added to 450 c.c. and 900 c.c., respectively, of normal saline or distilled water, a 5 per cent solution of glucose will be obtained. The glucose used shall be Merck's or Corn Products' or dextrose C.P. U.S.P.

A. 4000 gm. of glucose as specified are added to 8000 c.c. of fresh, triple distilled water of a

temperature of about 150° Fahrenheit, contained in a non-soluble glass container which has been washed and rinsed as ordered for flasks. The solution in flasks is heated in a double boiler—water bath with excelsior in bottom to protect outside of flask.

B. This is to be kept heated and agitated with a clean glass rod until the glucose is in solution.

C. Then 1 to 2 per cent by weight of powdered activated carbon is added to the warm solution of glucose and the whole well mixed by stirring with a clean glass rod. Finally replace double distilled water lost in evaporation before filtering. (*Avoid excess heat.*)

D. The solution while still hot is then filtered through one sheet of French filter paper previously wet with triple distilled water, using clean funnels of glass or block tin and caught in Erlenmeyer flasks washed and rinsed as in ¶ II. The first portion coming through is returned to filter No. 1 until it becomes clear. One *marked* flask is used to hold funnels when filter paper is being wet and for this purpose alone to avoid foreign particles.

E. This filtrate is filtered a second time in the same manner as in "D."

F. This second filtrate is filtered a third time as in "D."

G. The third filtrate is filtered a fourth time as in "D."

This fourth filtrate is measured in clean, prepared and graduated Erlenmeyer flasks, free of filter paper fibers, avoiding soiling of their mouths.

H. These flasks are to have their mouths covered immediately with unlacquered cellophane.

V. To make normal saline solution for intravenous use.

A. 8.5 gm. by weight of C.P. Merck's sodium chloride is added to 1000 c.c. of fresh triple distilled water contained in a non-soluble glass Erlenmeyer flask, washed and rinsed as in ¶. II.

B. This is agitated until a clear solution is made.

C. The solution is then filtered two times, separately, through one layer of French filter paper, previously wet with fresh triple distilled water each time and when solution is *clear*, collected in flasks cleaned as in ¶ II and graduated for 1000 c.c.

VI. To make 2 per cent saline solution for intravenous use.

A. Add 20 gm. by weight of Merck's C.P. NaCl to 1000 c.c. fresh triple distilled water.

B. Filter as normal saline, collecting in same way.

C. Put up in graduated Erlenmeyer flasks graduated for 1000 c.c.

VII. To make up sterile fresh triple distilled water for making solution for intravenous use.

Collect in graduated clean non-soluble glass flasks, prepared as in ¶ II in quantities most easily used.

VIII. All vessels or apparatus coming in contact with solutions shall be prepared and cleaned according to the requirements laid down for cleaning flasks.

No cleaning devices shall be used inside flask which might leave foreign particles sticking to inside of glass.

IX. For closing flasks:

A. The proper amount of the solution is put into the flask and a gum rubber stopper previously prepared is inserted into the mouth of the flask and tied in with twine, a loop of which comes over the top of the stopper so that it cannot slip out of the flask.

B. A piece of unlacquered cellophane (5″ × 6″) is placed over this stopper.

C. A piece of powder paper (4½″ × 6″) is placed over the cellophane paper and tied about the mouth of the flask with string.

X. Preparation of stoppers:

A. Only pure gum rubber stoppers are used.

B. The stopper has two perforations.

Insert a length of pyrex pressure glass tubing (8″ or 10″ long according to size of flask used) through one perforation so that the top of the tube is just below the level of the top of the stopper.

C. Insert a short right angle glass tube of the same material through the second perforation in the stopper. The length of this tube should be such that the lower end of the vertical arm will project ½ inch below the bottom of the stopper and the horizontal arm will lie upon the top of the stopper. The length of the horizontal arm should be such that it will not project beyond the rim of the flask when it is turned across the first perforation.

XI. Labeling flasks.

A. Glucose is tagged with a *white label*, marked as follows:

Sterile 000 c.c. 00% Glucose Solution in H_2O
(or normal saline) for Intravenous Use.
Date_____ Batch_____
Inspector_____

B. Normal saline tag with *green label*, marked as follows:

Sterile—000 c.c. 0.85% Solution NaCl
for Intravenous Use.
Date_____ Batch_____
Inspector_____

C. 2% Saline Solution, *orange tag*, marked as follows:

Sterile 1000 c.c. of 2% Solution of NaCl
for Intravenous Use.
Date_____ Batch_____
Inspector_____

D. Sterile triple distilled water with *red tag*, marked as follows:

000 c.c. Sterile Triple Distilled Water for
Intravenous Use.
Date_____ Batch_____
Inspector_____

XII. Sterilization of glucose solution by autoclave method, without vacuum. All solutions are sterilized immediately upon closing the flasks as described in ¶ IX.

1. The flasks are to be put in pressure sterilizer.
2. The door is closed and locked.
3. The upper and lower air pet cocks on door are opened to let air out.
4. The steam is turned into chamber.
5. When air coming from pet cocks changes to steam, close pet cocks.
6. When chamber gauge registers 5 lb., start time and run at 5 lb. for forty minutes.
7. At end of forty minutes of 5 lb. pressure, shut steam off chamber.
8. Open pet cocks on front of door and let steam escape *slowly* until pressure registers zero and no more steam escapes from open pet cocks.
9. Open door and let damp air escape, then remove flasks and put away in a dry place.

A, Normal saline, B, 2 per cent saline and C, triple distilled water are to be sterilized for fifteen minutes at 20 lb. pressure without vacuum or may be sterilized, for convenience, the same as glucose.

APPARATUS

The essential requisites for any apparatus used in giving infusions are:

I. It must be simple. This means that it should consist in as few parts and pieces as is possible. There should be no complicated parts which are difficult to clean or which require any preparation other than the standard technique.

II. It should be cheap; all parts should be easy to procure and economical to replace.

III. It should be durable and lasting.

IV. It should be simple and easy to operate.

V. It should prevent any contamination of the solution, even when the solution is kept for a long period of time.

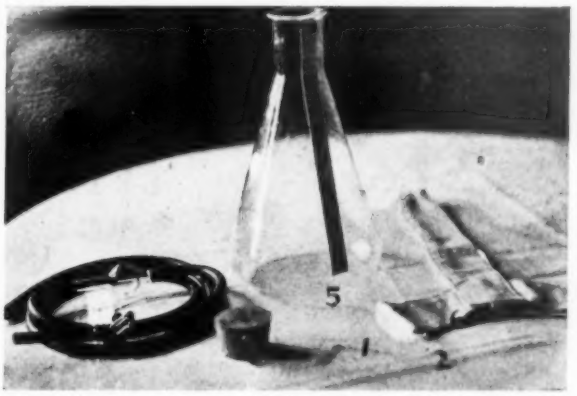

FIG. 1. Apparatus assembled. 1, Short right-angle glass tube which is inserted through top of rubber stopper. 2, Straight glass tube which is inserted through bottom of rubber stopper. 3, Rubber stopper. 4, Gum rubber tubing with Murphy drip bulb. 5, Flask graduated on outside. 6, Canvas sling for holding flask upside down.

The apparatus which we are using consists in an Erlenmeyer flask and gum rubber stopper with two glass tubes closed as already described and as shown in the illustrations.

When the flask is closed and sterilized according to the foregoing technique, it may be kept for a long period of time without having to be resterilized. If desired, it can be resterilized without being taken apart.

In developing this technique and apparatus, our idea was to eliminate all chance of the solution becoming contaminated from the time of the autoclaving to the time of its actual entrance into the vein. Nothing is inserted into the flask after it is autoclaved; the solution is not transferred to a gravity bottle and is

not exposed in the ordinary manner to the dust of the air.

The tubing is gum rubber and all glass

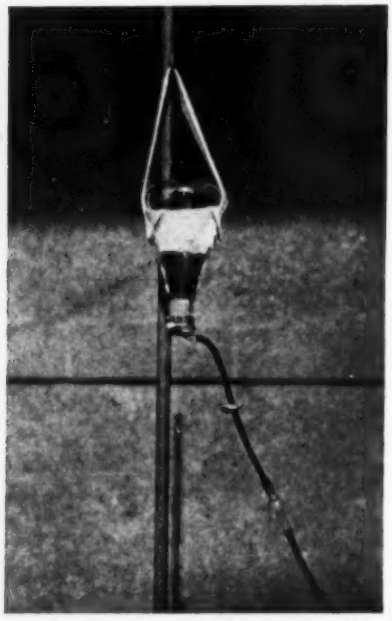

Fig. 2. Apparatus assembled ready for use.

connecting tubes, Y tubes and bulb droppers are of hard or non-soluble glass.

In using the solution, the flask is put into a water bath of ordinary cold tap water which is heated to 150°F. At this temperature the solution in the flask will be about 120°F.

The wrapper is taken off the flask, and the short horizontal glass tube is turned so that it projects beyond the edge of the flask and the free end of the rubber tubing is slipped over this glass tube.

A canvas sling is put over the flask in such a manner that the flask hangs upside down and the sling is hung at whatever height is desired. The air is expelled from the rubber tubing which is then clamped until connected to the needle which is now inserted into the vein and fixed with a small piece of tape.

The rubber tubing which connects the flask and the needle has a Murphy drip bulb through which the solution may be seen to pass.

The importance of the exact number of cubic centimeters or drops given per minute has been somewhat overemphasized in this manner: as measured in drops, the solution may be given as slowly as is desired but it may also be given as fast as desired provided the solution is always dropping and not running. In other words, we believe that in giving the solution intravenously, the speed is within safe limits as long as each individual drop can be seen and counted.

Within this limit it is desirable to give solutions of greater concentration at a slower rate than solutions of weaker concentration, to enable the tissues to take up and utilize the contents of the solution.

This apparatus allows the solution to go from the autoclave to the vein without any mixing, without any changing to another container, without any exposure to the dust of the air, and eliminates all possible chance of contamination. It is economical, easy to clean and set up, and simple in its operation.

The canvas sling, which holds the flask inverted, is made of strips of canvas 2½ inches wide and is fashioned so that it will fit the different sized flasks holding either 500 c.c. or 1000 c.c.

CONCLUSIONS

The known causes of reactions following intravenous infusions are reviewed and methods for eliminating the reactions are given.

In the majority of instances, following infusions, the temperature tends to remain stationary or to be slightly decreased.

A routine standard technique is given for the preparation of infusion solutions and apparatus.

A simple apparatus for the administration of these solutions is described.

I wish to express my appreciation to Dr. L. H. Loizeaux and Dr. Sprague Carleton, members of this Committee, for their help, and to Dr. Donald Gordon for his patient assistance and coöperation.

[For References see p. 85.]

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EDITORIAL

COMMENTS ON "THE X-RAY GALL BLADDER"*

SINCE Dr. Burden states that the surgeon has never seen the gall bladder contract, as a point of information I should like to point out that four surgeons have reported that they have seen the human gall bladder evacuate, two of whom claim that they saw the gall bladder contract, rather than simply collapse.[1]

Dr. Burden's interpretation of the muscular hypertrophy observed in some chronically diseased gall bladders, in which it is not due apparently to a secondarily contracted (fibrosis) gall bladder, as being due to "work hypertrophy" is quite interesting. We have observed a similar muscular hypertrophy of the gall bladder in some dogs with a stricture of the common duct.

Dr. Burden has emphasized the fact that the sphincter of Oddi is the most important factor concerned in the filling of the gall bladder. Other physiologic factors which must be considered are the tone and motility of the duodenum, the elasticity of the gall-bladder wall, the tone of the gall-bladder musculature, and the tone of a sphincter which probably exists at the junction of the cystic duct and gall bladder. If the gall bladder is able to be visualized, the obvious conclusion is that it fills and concentrates. If the gall bladder is not able to be visualized, the liver may

[1] Ivy, *Medicine*, 11: 345, 1932.

* See p. 60 of this issue.

not adequately eliminate the dye, or the gall bladder may not fill, or concentrate. Although experimentally the acutely inflamed gall bladder may be visualized, this does not usually happen; neither does it evacuate. Although such a gall bladder in the dog may be filled with contents of low specific gravity, the failure of such a gall bladder to be able to be visualized may be due to its failure to fill adequately with iodized bile. However, its inability to fill with iodized bile may be due also to its inability to concentrate the contents already in its cavity.

It is agreed experimentally that the gall bladder, in spite of chronic pathologic changes in its wall and mucosa, may fill, concentrate and evacuate.[2] In some instances, it may not. Dr. Burden's opinion that in such instances the sphincter of Oddi may be incompetent, or at least the gall bladder may not fill, may be correct.

One of the results of loss of gall bladder function is an incompetent sphincter; the other is a competent sphincter with dilated ducts. That a normal gall bladder may coexist with an incompetent sphincter is theoretically possible, but not likely.

A. C. Ivy.

[2] Murphy. *Ann. Surg.*, 20: 756, 1930; 21: 300, 1930. Darnbacher and Sacks. *Radiology*, 17: 538, 1931.

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WILLARD PARKER

[1800-1884]

The American Journal of Surgery
N.S. Vol. XXII, October, 1933

AMERICAN PHYSICIANS

WILLARD PARKER

WILLARD PARKER was born at Lindborough, N. H., September 2, 1800. He spent his boyhood in Chelmsford, Mass. He taught school in order to earn money for an education. He entered Harvard University and graduated with the class of 1826. While in Boston he saw Dr. John Collins Warren reduce a strangulated hernia and this gave him the urge to study medicine. Accordingly, he received a position as an interne at the Marine Hospital in Chelsia at $12.00 a month. After two years' study he received his medical degree from Harvard, 1830.

After graduating he went to Windsor, Vt., to teach surgery in the new medical school there. Later he was appointed professor of anatomy in Berkshire Medical College at Pittsfield, Mass. There he met Alonzo Clark, Elisha Bartlett and Robert Watts, later professors in the College of Physicians and Surgeons, New York City.

In 1836 he went to Cincinnati as professor of anatomy. In 1837 he went abroad to study, and the same year, after returning from abroad, he went to New York to occupy the chair of surgery at the College of Physicians and Surgeons. He held this chair until 1859. He started to practice and for many years enjoyed a large clientele.

With James R. Wood he reorganized the Almshouse at Bellevue into a hospital at which he was an attending surgeon. He was appointed attending surgeon to New York Hospital (1850); and later to a similar position on the staffs of St. Luke's, Roosevelt and Mount Sinai Hospitals. With John O. Stone he organized the New York City Department of Health. In 1856 he was elected President of the N. Y. Academy of Medicine. In 1870 he resigned his teaching position and was made Emeritus Professor. The same year Princeton University conferred upon him the degree of Doctor of Laws.

He was one of the most successful operating surgeons of his time. He was the first to do a cystotomy (1850). He tied the subclavian artery five times. In 1864 he ligated the left subclavian artery, inside the scalenus, together with the common carotid and subclavian arteries for subclavian aneurysm. It has been said he was the first in this country to lead the way in the proper treatment of appendicitis (1864), not knowing that Hancock of London had done a successful appendectomy in 1848.

Parker introduced the clinical lecture into college teaching.

He collected a valuable and wonderful library, which after he died went to the Library of the Medical Society of the County of Kings, Brooklyn, N. Y. This library received some 4000 volumes, many of them priceless.

Probably his greatest tribute was the building of a hospital for infectious diseases in New York City, which was named after him, The Willard Parker Hospital.

He married twice. By his first wife he had two children. His second wife, a widow, increased the family by a son and two daughters.

Seeing private patients to his last day, he was stricken with a cerebral hemorrhage and died in New York City, April 2, 1884.

T. S. W.

[From Fernelius' Universa Medicina, Geneva, 1679.]

BOOKSHELF BROWSING

HISTORICAL SURVEY OF ENDOSCOPIC PROSTATIC RESECTION*

R. GUTIERREZ, M.D., F.A.C.S.

NEW YORK

INTRODUCTION

OBSTRUCTION to the outflow of urine, and instruments to relieve this condition, have been known to exist since prehistoric days, long before the Christian era and the beginning of medicine, but the true pathological conception of vesical neck obstruction in its various phases was not then known or clinically recognized, and the subject remained in a distressing state of confusion for many centuries.

For the purpose of a historical review of this extremely interesting phase of urologic investigation, we may arrange the various periods into two essential groups: the Ancient and the Modern Periods.

ANCIENT PERIOD

According to Civiale (1841)[1] who was among the most noted genitourinary surgeons of his day, the idea of carrying a cutting or piercing instrument into the urethra either to open a way for the outflow of urine or to facilitate the dilatation of contracted parts, or even to form a new channel, must have presented itself at nearly the same time as the idea of having recourse to sounds or bougies during the early days of medicine and science.

Hippocrates, Galen and Celsus[2] in fact speak of "callosities" of the urethra which were destroyed by means of a catheter. Amatus Lusitanus (1557)[3] tells us that, long before his time, when bougies failed to pass they were raveled out at the end in order to make them engage with greater ease. John de Vigo (1460)[4] speaks of "forced catheterism," as does also Alphonse Ferri (1553)[5] in no uncertain terms. Tolet (1693)[6] relates that "carnosités" in the urethra were scraped and many other early writers have also stated that urethrotomies for the relief of strictures or obstructions and perineal lithotomy for crushing stones using the *grand appareil*, or the *petit appareil*, have been in use since the prehistoric days of medicine.

All these references are more or less vague and lack precision, and it is not until we come to Ambroise Paré[7] during the years 1510 to 1590 that we find the description of a definite operative pro-

* Read before the Section of Genito-Urinary Surgery, New York Academy of Medicine, April 19, 1933. An abstract from the author's original article, "Transurethral Treatment of Bladder Neck Obstruction—Endoscopic Prostatic Resection," in Dr. Bransford Lewis' book on the History of Urology.

cedure in which a sound with several sharp ridges on its surface, one fingerbreadth from its tip, was inserted in the urethra and turned this way and that, until the obstruction was overcome. Far from fearing hemorrhage, Paré actually invited it, encouraging the "carnosité" to bleed and thereby "discharge part of itself," with a view to shortening the duration of the treatment. His catheter, terminating in a hemispherical button with a cutting edge, was designed to pick up and crush the obstruction to any desired degree at a single sitting. It is evident that Paré had, in the sixteenth century, the very ideas which were put forth in the first half of the nineteenth century, such as that of scarification and of passing and withdrawing the bougie after it had cleared the obstruction, and then repeating the same procedure on different occasions. The fenestrated cannula of Paré has served as the model for several later rongeurs. Lacuna of Rome[8] in 1560 also wrote a book entitled "Methodus cognoscendi extirpandique in vesicae collo carunculas" (A method of recognizing and extirpating caruncles in the neck of the bladder). "Carnosité" and "caruncula" or "engorgement" were the loose names given to the prostate until Riolan baptized it with the name of prostate gland.

We also learn from Civiale[1] that operations designed to puncture strictures or carnosités of the urethra were sufficiently in vogue at the end of the sixteenth century to make the Faculté de Paris think it ought to interfere: so that on December 5, 1603, it passed a vote of censure against Turquet de Mayerne[9] as unworthy to practice the art of healing "*propter temeritatem, impudentiam et ignorantiam*," which, however, did not prevent him from becoming a man of great learning, to whom the King of England entrusted the care of his health.

The type of instruments used by these early surgeons and the mode of operation have not come down to us. The stories with regard to them are too incomplete for any authority to be attached to them but it can be safely asserted that the transurethral approach to the bladder was known from very early times, and there are records of procedures of this kind being carried out with full confidence, in grave cases, even upon eminent members of the medical profession. Thus it is recorded that in 1726 the life of Astruc, who was suffering with a tumor of the neck of the bladder, was prolonged for ten years by La Faye (1736),[10] whose instrumentation and technique did not differ in any marked degree from those used in the nineteenth century for impassable contractures and obstructions of the bladder neck. He used a sound of usual curvature, open at both ends, which could be made to pass beyond the end of the cannula for a distance of 8 mm. As soon as this point, which was drawn back into the sound, had reached the obstacle, the surgeon inserted a finger into the rectum and pushed the stylet forcefully—after which, the bladder having been reached, he withdrew the stylet and left the sound in place for a few days. On La Faye's[10] instrument were modeled others used by Physieck,[11] Doerner,[12] Stafford[13] and others who were the chief promoters of the method during the years 1768 to 1829. All these instruments were more or less alike, varying only in such details as the amount of curvature, the cutting or piercing nature of the operating end, the greater or lesser projection of this from the cannula, and the emergence of this tip from its sheath by simple pressure, or by a spiral or other device.

MODERN PERIOD

During the modern period we must take into account three eras.

First Era: The first comprised the early days when the anatomical conception of the third lobe of the prostate was described and considered as an independent unit in the evolution of prostatic hypertrophy. It was also the beginning of a new conception of the median bar or bladder neck obstruction as the potential cause of

retention and the resulting surgical pathology. To this period, covering the first half of the nineteenth century, are attached the names of Guthrie (1830),[14] Home (1806),[15] Henry Thompson (1857),[16] Charles Bell (1812),[17] Civiale (1841),[1] Mercier (1841),[18] Leroy d'Étiolles (1849),[19] Velpeau (1841),[20] Béniqué (1838),[21] Rochet (1859)[22] and others. These men had the glimmerings of the true clinico-anatomical conception of the "maladie des vieillards," and they inaugurated an era with a sounder basis for transurethral instrumentation, although in the dark, in an effort to relieve the mechanical obstruction at the bladder outlet. Many ingenious instruments were devised. Almost every author had an instrument of his own, which they variously called the prostatome, the incisor, the excisor, the prostato-lithotrite, the kiotome, and many other like names. Later on, among other instruments, the Bottini galvanocautery in 1874 was introduced with its many modifications, and obtained considerable success.

Thus it was a little over a century ago that the nature and treatment of bladder neck obstructions became for the first time the subject of serious scientific study, through the investigations of Everard Home (1806)[15] and the work of George James Guthrie,[14] a distinguished English surgeon whose name occupies a significant place in modern urology. It was Guthrie[14] who in 1830 first described under the title of the "The Bar at the Neck of the Bladder" a condition whose pathology and treatment now constitute one of the most debated questions in the entire field of urology. Guthrie[14] was the first investigator to describe non-prostatic obstruction of the outlet of the bladder. In a lecture that was one of a series delivered before the Royal College of Surgeons in London, he laid down two important propositions, as follows:

1. That the elastic structure at the neck of the bladder may be diseased without any necessary connection with the prostate gland.

2. That the prostate may be diseased without any necessary connection with the elastic structure.

Guthrie[14] thus established a differentiation between hypertrophy of the glandular tissue of the median lobe and the "bar at the neck of the bladder." The transurethral operation he regarded, in the state of knowledge then current, as applicable only in the case of the bar.

The instrument used by Guthrie[14] was made by Everill and Mason, as an improvement on the central perforator or lancet of Stafford, rendering it capable of cutting on the side, and of being easily cleaned. It was characteristic of Guthrie that he wished the instrument to be called by their name, keeping for himself only the credit of having made the suggestion. This instrument consisted of a metal bar curved like a No. 20 F. prostatic catheter, carrying at its extremity a small concealed knife, which was made, by means of a spring, to project by the side, or by the end, or by both, as far as might be thought advisable. Guthrie's farsighted wisdom in his conservative attitude toward his method cannot but command our admiration and puts to shame the trivial squabbling for priority that was to follow on the part of certain later workers.

The importance of Guthrie's work was denied by the French surgeon Mercier[18] in an article published in 1836, followed by other articles in 1839 and 1841, which gave specific descriptions of Mercier's own operative methods and discoveries, discounting everything done by anyone before him in the exploration or treatment of the prostate. In a work entitled "Recherches sur les valvules du col de la vessie" (Researches with reference to the valves at the neck of the bladder), Mercier put forward his own claim to priority.

Mercier likewise disregarded the work done in this field by Home,[15] who in 1806 had laid before the Royal Society a paper entitled "An Account of a Small Lobe of the Human Prostate Gland which has not

before been taken Notice of by Anatomists," in which he described a nipple-like projection of the prostate forming a valve-like obstruction to the outflow of urine, the so-called third lobe of the prostate or median lobe hypertrophy.

When Mercier had disposed of his English rivals, he attacked his own compatriot, Civiale, who, twenty years his senior, published a treatise on "Diseases of the Genito-Urinary Organs" in 1841 in which he gave a clear description of a non-prostatic obstruction of the bladder neck, of which he identified three types, giving also a long and thorough account of their etiology and treatment. In Mercier's next book he flayed Civiale in a long letter addressed to him, preceding the text, in which he openly accused him of plagiarizing his own observations. He also attacked him from time to time in many other publications.

In our own day Randall,[23] who has written the history of this episode in some detail, has thus admirably summed up Civiale's reaction:

> Civiale's only reply to his accusation of plagiarism was a short letter written in the calm terms of a man of broader mind. He couched his letter in the form of three questions, each of which he answered as follows: Did Mercier question his originality? He asserted none, and stated that the priority belonged to some English surgeon. Did Mercier criticize the exactitude of his descriptions? Civiale says: "I never pretended to lay down a limit to science: I have but described what I truly saw!" Did he dispute his treatment? "From that point of view experience alone ought to speak."

Mercier confessed that he had some trouble with hemorrhage, but claimed that he had never yet failed to overcome it, and that his experience covered 300 cases. He regarded "incision" as a greater source of danger than "excision" since the vessels were crushed more in the latter process. For his "prostatic variety" of obstruction, he advocated excision, removing three portions, a median and two lateral ones; but for the "muscular variety" he regarded incision as the correct course. There is every evidence that Mercier obtained very good results from his operative procedures; numbers of his patients willingly returned for further treatment, thus expressing their satisfaction with the relief he had given them on a former occasion.

There was a lapse of some thirty years from the time of Mercier's work before we hear of fresh undertakings in this field.

In 1873 Hutchinson[24] came to the disheartening conclusion that all methods of overcoming prostatic hypertrophy were ineffectual; the only resource, in his opinion, was the permanent catheter and this was almost sure to cause cystitis.

In 1874, however, Bottini[25] introduced his galvano-cautery designed to act not merely upon the mucous membrane, as Mercier's instrument could do, but capable also of producing thermogalvanic destruction and incision of the morbidly enlarged lobe of the prostate to any extent.

Musati, a physician upon whom Bottini did an operation, said of it: "The pain is so easily borne that I would advise everyone against the use of chloroform. I can place on record that I have suffered more with burning of the prostate by silver nitrate than during the galvanic division."

Bottini's method had the advantage over Mercier's instruments of not producing hemorrhages, and during the next twenty years it attained considerable vogue. Designed by Bottini to relieve prostatic hypertrophy, there can be no doubt that the instrument did some of its best work in cases of median bar formation.

The danger of too destructive action in the dark, however, caused most surgeons to fear to employ Bottini's procedure, with the result that in 1897 Freudenberg[26] made certain improvements designed to overcome its danger and to achieve greater accuracy of application. He even invented a visual cautery instrument by combining Bottini's galvanocautery blade with the irrigating cystoscope which had now come into use.

Meantime Harrison (1884),[27] Gouley (1885),[28] Norton (1892)[29] and others had been using Mercier's procedure but had carried it out through a perineal incision, all using instruments of their own.

In 1892 W. N. Wishard,[30] of Indianapolis, reported that he had for two years been applying the cautery through a median perineal opening with the operative area under direct observation. Ten years later in 1902 he developed an instrument for this purpose and included in his method the use of the Kock air-dilating cystoscope through the perineum, which was later employed through the natural channel.

Chetwood[31] in 1905 reported a series of 36 cases in which he likewise had performed a perineal buttonhole operation. With an instrument of his own, he modified the Bottini-Freudenberg procedure, providing better control of bleeding as well as more accurate diagnosis by palpation of the bladder neck. This Chetwood procedure was widely generalized during the early part of the twentieth century, and many interesting reports were published. Among the early advocates of this method appear the names of Keyes,[32] Bangs,[33] Willy Meyer,[34] Newman,[35] Fuller,[36] Nitze,[37] Watson,[38] Wishard,[30] Bransford Lewis,[39] Young,[40] Guitéras,[41] Texo[42] of Buenos Aires, Menocal[43] of Havana, Cunningham of Boston,[41] Deaver[45] of Philadelphia, Belfield[46] of Chicago, Pedersen[47] of New York and a host of others.

In France, Legueu,[48] André,[49] Cathelin,[50] Pasteau,[51] Minet,[52] Desnos,[53] Albarran[54] and others regarded the method as useless or too dangerous to be risked, and it never came into general use in that country. It appears also that the technique of prostatectomy was so rapidly advancing both here and abroad, and was achieving such brilliant results, that the Bottini and Chetwood methods soon passed into oblivion. The procedure, however, had its relative merits and historical interest, although it did not stand the test of time.

Second Era: The second era of this modern period was inaugurated with the work of Albarran,[54] who revolutionized the ancient anatomic conception of the obstructing bar and the so-called third lobe of the prostate. He described in a very lucid manner his clear-cut histo-anatomo-clinico-pathological conception of the subcervical group of glands of the bladder neck, which may undergo hypertrophy independently of the prostatic hypertrophy, causing dysuria and the clinical symptoms of prostatic disease. This important discovery became classic and since then bears his name. It prompted Guyon[55] and other writers to describe the so-called "*prostatisme sans prostate,*" which condition has remained as a classic entity in the literature since Albarran's time. More recently Legueu,[48] Marion[56] and other writers of the French school have described the so-called "*maladie du col de la vessie,*" which more graphically has been referred to as "*les dysectasies du col de la vessie,*" meaning clinically and anatomopathologically hyperplasia and hypertrophy of the glandular, muscular and sphincteric tissue and therefore embracing all the elements of the bladder neck.

This new conception of the nature of the obstructing condition at the vesical orifice has received considerable attention in the urologic world, both clinically and surgically, particularly since the advances of cystoscopy and endoscopy have made possible the direct observation and visualization of the bladder and urethra, not only for diagnosis, but also for their proper transurethral treatment. During this period also an exhaustive study was made of the frequency and variety of types of prostatic obstruction, as well as of the methods of prostatectomy, both the perineal and the suprapubic procedure, as the most efficient means of treating prostatic hypertrophy.

Third Era: The third era of this modern period, comprising the progress made since Albarran's discovery, embraces the perfecting of prostatectomy together with the transurethral use of the electric current for fulguration of tumors of the bladder,

introduced by Edwin Beer[57] in 1910, who was awarded a gold medal for his achievement at the Fourth Congress of the International Urological Association held in Brussels in 1926. The same principle was afterward applied to certain types of prostatic hypertrophy and bladder neck obstructions by Stevens,[58] Bugbee,[59] McCarthy,[60] Georges Luys[61] of Paris and Heitz-Boyer[62] and others, the so-called fulguration of the obstructing prostate.

In 1909 the instrumental era of endoscopic prostatic resection was inaugurated in America by Hugh Young[40] who introduced the so-called "punch operation" or "punch prostatectomy." To this era are attached the names of Young,[40] Caulk,[63] Geraghty,[64] Braasch,[65] Bumpus,[66] Collings,[67] Maximilian Stern,[68] T. M. Davis,[69] Foley,[70] Day,[71] Rose,[72] McCarthy,[60] Kirwin,[73] Mathé,[74] Ravish,[75] Redewill,[76] Ockerblad,[77] Alcock[78] and many others who are now using this method in selected cases for the relief of vesical neck obstructions. Abroad the endoscopic method has been used by Goldschmidt[79] and Wossidlo[80] in Germany, and by Georges Luys[61] in France, where it is known as "le forage de la prostate"; also by Kenneth M. Walker[81] in England, where the instrument is called the diathermy punch for perurethral operations for prostatic obstruction. The description of all these instruments will be found in my chapter, "Transurethral Treatment of Bladder Neck Obstructions—Endoscopic Prostatic Resection," to be published in Dr. Bransford Lewis' book on the History of Urology.

The transurethral method owes its resurrection or its improvement to the evolution of new instruments along this line and also to the introduction of the new electric current with high power, which makes it possible to cut the offending tissue and to coagulate any bleeding point under water and under direct vision through the sheath of an endoscopic tube. It permits the excision of a considerable amount of tissue and the more or less complete remodeling of the outline of the channel of the prostatic urethra and the vesical orifice. In this connection the enthusiasm of American urologists has been aroused by the innumerable ingenious devices made by the late Mr. Reinhold Wappler and his brilliant son Mr. Frederick C. Wappler, to whom our thanks are due for their aid in refining transurethral operations.

In closing this impartial historical survey, it seems permissible to remind the reader that, regardless of the achievements made and the progress accomplished in this electrosurgical and resectoscopic era with the revival of transurethral prostatic resection, we must not overlook the fact that the method does not prevent the recurrence of prostatic hypertrophy and that it does not, therefore, solve entirely the problem of the prostatic. The procedure in its modern refinement unquestionably has its merits and has met with good results when used in well-selected cases of vesical neck obstruction and prostatic obstruction. However, this endoscopic surgical operation, although minor in character and execution, is not always free from the danger of complications and fatalities. Hence, the future alone can make the final decision in this important battle. It is obvious that the procedure should always be performed by competent and well-trained cystoscopists and that the patient should receive the same preliminary preparation and postoperative care as in any routine case of perineal or suprapubic prostatectomy.

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[For Remainder of References see Author's Reprint.]

BOOK REVIEWS

THE JOY OF LIVING. An Autobiography. By Dr. Franklin H. Martin. 2 Vols. N. Y., Doubleday, Doran & Co., 1933.

Dr. Martin's autobiography might well be called "The Man Who Knew How to Overcome Obstacles." The work would seem to depict "The Joy of the Fight." There are two large volumes. The first carries us up to the World War and the second is devoted practically in its entirety to the History of America's Medical Activities during the World War as Seen and Participated in by the Author.

It is the history of a great executive—the man who never takes "no" for an answer. The surgeons of America well know that Dr. Martin has a habit of completing successfully every task he undertakes. The organization and success of the College of Surgeons is largely due to his personal efforts and perseverance. And this same perseverance combined with a love of hard work for work's sake are reflected from each page of this autobiography.

The first volume tells of his antecedents, his youth in what was then the wilds of Wisconsin, and relates step by step the development and growth of a prominent American surgeon who, in addition to that *sine qua non* of the successful surgeon, a splendid pair of hands, also had unusual executive ability. This he devoted not to the building of a great private institution or clinic, but to the organization of the world's largest surgical society, thereby doing "the greatest good to the greatest number."

The story of the organization of the College of Surgeons over the objections and petty jealousies of many individuals and institutions is interesting and worthy of record. The early career of this great surgical leader is a typical American story—a sturdy background, much character, but little money. The hardships faced and overcome were responsible for the success of Dr. Martin's later career.

Four dollars a month for a furnished room "with a red carpet" seems like a tale of the dim and distant past but it is what Dr. Martin and another young man paid for their lodging during their medical school days.

Country school teaching and a pride in interesting and getting the cooperation of students who had made a point of flaunting their previous teachers is part of the training that enabled Dr. Martin to get the surgeons of America to do pretty much as he wished despite all opposition. As tall oaks from little acorns grow, so our truly great national leaders seem to spring from little country school teachers. The story of Dr. Martin's rise to leadership is almost the conventional one of success through hard labor. And there is no better method of clinically teaching the way of life than by the case history method of presenting actual cases that have overcome difficulties that seemed insurmountable. A careful and consecutive reading of the volumes makes Dr. Martin's success seem inevitable. Step by step he kept going continually forward, working out all his problems by himself and never depending on "pull."

The first volume brings us up to the World War and is interesting from beginning to end. As stated before, the second volume is devoted largely to the history of the medical department during the War and is fully documented so as to furnish in reality a splendid reference work or source book on this subject. Interspersed as it is with personal anecdotes of prominent figures, it is of particular interest.

Dr. Martin has taken a definite place in the history of American surgery and we prophesy that his autobiography will become one of the classics of American literature. It should be in the library of every surgeon.

TEXTBOOK OF PHYSICAL THERAPY. By Heinrich F. Wolf, M.D. Foreword by Lewellys F. Barker, M.D. Chapters by William Bierman, M.D., Alolph A. Lilien, M.D., Farel Jouard, M.D. and Madge C. L. McGuinness, M.D. N. Y., D. Appleton-Century Company, Inc., 1933.

Though called a Textbook of Physical Therapy, this book seems to be essentially for the practicing physician.

The philosophy of physical therapy is splendidly brought out and it would seem that the work was intended particularly to aid the general practitioner to decide when to use physical therapeutics and to assist him in the choice of modality. Particular stress is laid on the necessity for correct diagnosis and the physiological principles of the therapy suggested are thoroughly explained. The discussions of "diagnostic therapy" will be found of considerable interest. There is no bibliography and there are few quotations, the work being based largely on the author's personal experience and it is refreshing to find an author who does not hesitate to express his opinions freely and clearly.

Chapters on Hyperthermia, Diseases of the Lower Respiratory Tract, Otolaryngology, Minor Electrosurgery and Gynecology are contributed by specialists, the author admitting frankly his lack of experience in these lines.

The work is thoroughly practical, conservative and up-to-date. It is a welcome addition to the literature on this increasingly important subject.

Sex and Internal Secretions, A Survey of Recent Research. Ed. by Edgar Allen, M.D. Foreword by Robert M. Yerkes, Sc.D., 21 Contributors. Balt., Williams & Wilkins Co., 1932.

According to the Foreword by Robert M. Yerkes of Yale, this volume with 21 contributors, edited by Edgar Allen, is a survey of ten years "of research on fundamental problems of sex under the administrative guidance of a committee of the Division of Medical Sciences, National Research Council." The purpose of this book is "to survey the most important recent researches in problems of sex, especially those concerned with internal secretions, in order that the concepts already established by experimental evidence may be clearly stated and made readily available." The entire subject being still covered by a haze of obscurity and doubt, it is good to have an authoritative discussion of the present status of the situation at hand.

There are 19 chapters, each written by a specialist of rank.

The biological aspects of the question are thoroughly covered. It differs from the usual book on sex in that the sociological aspects are not considered. Gynecologists and endocrinologists will find this book a valuable work of reference.

A Synopsis of Surgery. By Ernest W. Hey Groves, M.D. Ed. 10, N. Y., William Wood and Co., 1933.

Ten editions since 1908 bespeak the well-merited popularity of this work. According to the author: "It is thought that this synopsis may, by its methodical arrangement, prove of assistance by presenting the diagnosis and treatment of surgical conditions in a concise manner." This it certainly does and the work is to be highly recommended as a desk companion for every surgeon. Here will be found quickly just the points which are needed and which often require much browsing to be obtained from the large systems and treatises.

Rose and Carless' Manual of Surgery. Revised by Cecil P. G. Wakeley, D.Sc., and John B. Hunter, M.C. American (14th) Ed. Ed. by W. T. Coughlin, M.D. Balt., William Wood and Co., 1933.

The fourteenth edition of Rose and Carless' Manual of Surgery now comes to us in an "American edition," edited by Dr. W. T. Coughlin of St. Louis. Where differences in practice occur in England and America, the English practices have been discarded and the American substituted so that the book which always has been a valuable textbook may now be considered as especially adapted to American schools.

Gynecology for Nurses. By George Gellhorn, M.D. Ed. 2, Phila., W. B. Saunders Co., 1933.

This book has been brought thoroughly up-to-date and covers in 28 chapters, concisely and authoritatively, just the information that the gynecological nurse needs. As a textbook and as a handbook for nurses, this book is thoroughly practical. Questions at the end of each chapter are well selected. The nurse who can answer these correctly may be considered well fitted for her job.

Obstetrics and Gynecology. By Arthur H. Curtis, M.D. Vol. 2. Phila., W. B. Saunders Co., 1933.

The second volume of this excellent work continues the pace set by Volume 1. Last month we told our readers it was of a high order and urged all interested to procure the set. We can do no more than repeat our praise.

In this Volume the Pathology of Labor, Pathology of the Puerperium, Operative Obstetrics, Infectious Processes, and Tumors of the Uterus are considered. Under each heading various authors contribute. We cannot find fault with any of them. We would, had we the space, tell about each and all of them. We particularly liked Stander's chapter on Cesarean Section. Howard Kelly writes a brief outline of the history of American Gynecology which is different from most historical reviews; he never has done a finer bit of writing than in this short chapter.

Again we must bow to Dr. Curtis who has done a meritorious and skillful piece of editing. The third volume will appear shortly. A high class, sound, solid, satisfying work.

ACUTE INTESTINAL OBSTRUCTION

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TENTH INSTALLMENT

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Chapter XXVII

MORTALITY

It is generally recognized that acute intestinal obstruction is an extremely serious disease; the mortality, even under modern conditions, is high. From a historical standpoint, the figures on mortality given by the early writers (Ashhurst,[1] Curtis,[2] Fitz,[3] and Gibson[4]) are of interest; since, however, they were not based on consecutive cases but on cases selected from the literature, they really give no accurate information. Even in more modern reports it is difficult to arrive at an accurate estimate of the mortality because of the complexity of the picture presented by the disease and the number of factors affecting the mortality. Comparison of the figures from various clinics is somewhat confusing, for the several surveys include different groups of cases: one study, for example, may omit obstructions from carcinoma, another may exclude cases complicated by peritonitis; and such differences greatly affect the statistics.

Table xvii

MORTALITY FROM ACUTE INTESTINAL OBSTRUCTION AS REPORTED FROM VARIOUS CLINICS*

Author	*Year of Report*	*Number of Cases*	*Mortality (Per Cent)*
Scudder[6]	1907	121	60
McGlannan[7]	1913	181	37
Deaver and Ross[8]	1915	276	42
Codman[9]	1920	41	34
Richardson[10]	1920	118	41
Braun-Wortmann[11]	1924	379	39
Souttar[12]	1925	3064	32
Tuttle[13]	1925	150	50
Brill[14]	1929	124	36
Miller[15]	1929	343	61
Smithies[16]	1930	56	41
McIver[5]	1931	156	44

* Since the different series include somewhat different types of cases (certain of the series, for example, include strangulated external hernias while others do not) the figures are not strictly comparable. (McIver.[5])

If we bear in mind that they are not always closely comparable, the statistics from different clinics are nevertheless of importance as indicating a high mortality. Table XVII gives representative figures which have appeared in the literature. Although there is considerable range in the percentage of mortality shown by the different authors, apparently the disease has proved fatal in almost half the cases. Miller,[15] in his recent study of intestinal obstruction in various hospitals of New Orleans, comes to the conclusion that if the figures commonly given are rigidly revised to include only acute, complete obstructions, they show a mortality of from 50 to 65 per cent, whereas they are usually stated as from 30 to 40 per cent.

Factors Affecting Mortality: Based on Figures from the Massachusetts General Hospital

An analysis of all cases of acute intestinal obstruction at the Massachusetts General Hospital during the ten-year period 1918–1927[5] has brought out the mortality figures, shown in Table XVIII, which will be briefly discussed.

Table XVIII

MORTALITY IN 335 CASES OF ACUTE INTESTINAL OBSTRUCTION FROM ALL CAUSES, TEN-YEAR SERIES, MASSACHUSETTS GENERAL HOSPITAL (MCIVER[5])

Classification	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*
Group I. (All cases of acute mechanical obstruction except those due to neoplasms or to strangulated external hernias)	156	68	44
Group II. (Obstructions due to neoplasms)	32	10	31
Group III. (Obstructions due to strangulated external hernias)	147	27	18
Total all causes	335	105	31

TABLE XIX

MORTALITY IN DIFFERENT TYPES OF CASES, THIRTY-YEAR SERIES*

Type of Case	1898–1907			1908–1917			1918–1927		
	Number of Cases	*Number of Deaths*	*Mortality (Per Cent)*	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*
Early postoperative (within 4 weeks after operation)	18	13	72	29	7	24	37	17	46
Late postoperative (more than 4 weeks after operation)	19	6	32	28	11	39	45	13	29
Bands and adhesions without previous operation	33	18	54	14	7	50	21	9	43
Meckel's diverticulum	9	7	78	4	2	50	2	0	0
Volvulus	9	9	100	16	4	25	13	6	46
Intussusception	27	14	52	20	12	60	17	9	53
Mesenteris thrombosis	1	1	100	5	4	80	9	9	100
Congenital anomaly	2	2	100				2	2	100
Gallstone or other foreign body	1	1	100	1	1	100	7	2	29
Strangulated internal hernia	2	2	100	1	1	100	3	1	33
Total	121	73	60	118	49	41	156	68	44

* Table XIX shows the mortality in different types of acute intestinal obstruction (exclusive of those caused by strangulated external hernia or by neoplasms). In making a comparison of the three 10-year series, 1898–1927, Massachusetts General Hospital, it will be noted that there was a definite improvement between the first and second periods; but that the figures for the second and third periods are strikingly similar: while there has been improvement in some types, in other types the figures are less favorable. (Scudder,[6] Richardson,[10] McIver.[5])

GROUP 1. Group 1 includes all cases of acute mechanical obstruction except those due to neoplasm or strangulated hernia. Owing to previous studies by Scudder[6] and by Richardson,[10] the mortality figures in these types of obstruction at the Massachusetts General Hospital are available for the past thirty years, and are shown in Table XIX.

In the analysis of these cases of intestinal obstruction, all deaths during the hospitalization, whether or not the direct result of the obstruction, were included. The cases were grouped according to the most important feature of each, and since certain cases have characteristics allying them to more than one type, the final arrangement must be considered as somewhat arbitrary.

A contrast of the different ten-year periods is interesting; while there was a definite improvement between the first and the second periods the figures for the second and third periods are strikingly similar: there has been improvement in some types, while in other types the figures are less favorable.

In considering the factors that affect the mortality of this group, certain ones stand out predominantly: (1) the length of time elapsing between the onset of the acute obstruction and its relief by operation; (2) interference with the circulation to the bowel, and (3) the age of the patient.

Time Element. The time elapsing before operation is perhaps the most important factor affecting mortality, for if sufficient time has elapsed for marked damage to the bowel to have occurred and for systemic effects to have manifested themselves, surgery is often unable to prevent a fatal termination even though the obstruction be relieved. The relation of the time element to mortality is shown for the 1918–1927 series in Table XX.

There were 149 cases in which it was possible to estimate approximately the duration of symptoms before operation. About half the cases (73) were operated on within the first forty-eight hours, with a mortality of 26 per cent; the remainder,

operated on beyond that period, showed a mortality of 60 per cent.

TABLE XX

RELATION OF MORTALITY TO DURATION OF SYMPTOMS BEFORE OPERATION*

Duration of Symptoms	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*
Less than 24 hours	36	6	17
24–48 hours	37	13	35
Over 48 hours	76	46	60

* About one-half the cases (73) were operated upon within the first forty-eight hours, with a mortality of 26 per cent. The remaining half, operated on beyond that period, showed a mortality of 60 per cent. This illustrates in striking manner the importance of early diagnosis and operation in cases of acute obstruction. (McIver.[5])

Interference with the Circulation to the Bowel: (a) Mesenteric Circulation. The amount of interference with the mesenteric circulation is a factor of greatest importance in determining the acuteness of the illness and the ultimate outcome; the greater the damage to the bowel the more marked the toxemia. This has been known for a long time, both from clinical observation and from experimental work (Bryant,[17] Murphy and Vincent[18]). Analysis of the recent Massachusetts General Hospital series brings out the validity of this point of view. Table XXI shows that 66 cases (or 42 per cent of the total number) had some degree of interference with the mesenteric circulation, although in many cases this was not extreme. The mortality in patients showing interference with the mesenteric circulation was 53 per cent, as contrasted with 37 per cent in patients not having this complication. Table XXII shows that about half the patients during the thirty-year period had interference with the mesenteric circulation, and that the mortality among them was 62 per cent as contrasted with a mortality of 41 per cent where the mesenteric blood supply was undisturbed. It is probable that these figures would be more striking but for the fact that where there is any element of strangulation present the onset of symptoms is

likely to be more fulminating and the pain often so extreme that the patient is brought early to operation; the favorable time element thus to some extent offsets the more serious pathological condition.

TABLE XXI

RELATION OF MORTALITY TO INTERFERENCE WITH MESENTERIC CIRCULATION*

Classification	*Number of Cases*	*Number Showing Interference with Mesenteric Circulation*	*Mortality in Cases with Interference (Per Cent)*	*Mortality Cases without Interference (Per Cent)*
Postoperative, early	37	2 (5%)	100	43
Postoperative, late	45	17 (38%)	29	28
Bands and adhesions without previous operation	21	8 (38%)	50	38
Meckel's diverticulum	2	2 (100%)	0	0
Volvulus	13	9 (69%)	55	25
Intussusception	17	17 (100%)	53	0
Mesenteric thrombosis	9	9 (100%)	100	0
Congenital anomaly	2	0	0	100
Gallstones and other foreign bodies	7	0	0	29
Strangulated internal hernias	3	2 (67%)	50	0
Total	156	66 (42%)	53	37

* It will be noted that in the obstructions occurring early after operation this complication is relatively infrequent; it is also rare in obstructions by neoplasms. (McIver.[5])

(b) Capillary Circulation. It is difficult to estimate statistically the relation of interference with the capillary circulation to mortality. Probably all cases where the obstruction has existed for any appreciable length of time show some interference with the capillary circulation, from distention, and resulting changes in the bowel wall.

Age of the Patient. It will be noted from Table XXIII that the age of the patient has a definite relation to the death rate, the

TABLE XXII

INTERFERENCE WITH THE MESENTERIC CIRCULATION, THIRTY-YEAR PERIOD (ALL CASES OF ACUTE OBSTRUCTION EXCEPT THOSE DUE TO EXTERNAL STRANGULATED HERNIA AND NEOPLASM)*

Period	*Number of Cases*	*Number Showing Interference with Mesenteric Circulation*	*Mortality in Cases with Interference (Per Cent)*	*Mortality in Cases without Interference (Per Cent)*
1898–1907	121	59 (49%)	78	57
1908–1917	118	54 (46%)	55	30
1918–1927	156	66 (42%)	53	37
Total	395	179 (45%)	62	41

* This table again illustrates the higher mortality shown by cases of obstruction complicated by interference with the mesenteric circulation. (Scudder,[6] Richardson,[10] McIver.[5])

TABLE XXIII

AGE IN RELATION TO MORTALITY*

Age of Patient	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*
Under 1 year	10	6	60
1–10 years	11	5	45
11–20	28	8	29
21–30	27	8	30
31–40	24	6	25
41–50	20	11	55
51–60	13	8	62
61–70	13	8	62
71–80	9	7	78
81–90	1	1	100
Total	156	68	44

* It will be noted that the mortality is especially high in the first decade and after the fifth decade. These figures do not include obstructions from strangulated external hernias or from neoplasms. (McIver.[5])

mortality being very high in those under one year, and also, in this series, in patients over fifty years of age.

Influence on Mortality of the Modern Treatment of Dehydration. The figures from the Massachusetts General Hospital were of especial interest in relation to the effect on mortality figures of the modern treatment of dehydration. During the last four years of the 1918–1927 period, several physicians in the clinic were especially interested in the value of normal salt solution in combatting dehydration, and every effort was made to see that all patients with intestinal obstruction received adequate treatment with salt solution. It was the general opinion that these measures were distinctly worth while and in a number of instances were life-saving procedures. When, however, the recent ten-year series as a whole was contrasted with the 1908–1917 series, no lowering of the total mortality was found; also, when the mortality of the last four years of the present study was contrasted with that of the first six years, no reduction was found. This can probably be explained by the following facts. First, as pointed out by McIver and Gamble,[19] simple high obstruction in humans (the only type comparable to the experimental obstructions in animals in which salt solution is so efficacious)* is a relatively rare occurrence; this is borne out by the figures in Table XXIV, which show that only 2 per cent of obstructions were situated in the upper jejunum. Second, where damage to the bowel exists, due to interference with the circulation, the factor of dehydration is relatively unimportant, for the disease runs such a rapid course that the extreme degree of dehydration and loss of chloride and sodium ions does not have time to develop. In this group, 42 per cent (if strangulated hernias and neoplasms are included, this figure rises to 63 per cent) of the cases showed some interference with the mesenteric circulation, and there were a number in which damage to the capillary circulation by distention undoubtedly played an important rôle. Thus in the great majority of cases

* As shown by Hartwell and Hoguet, and numerous other experimenters, when dogs with simple high obstruction of the jejunum are treated with sufficient quantities of salt solution to replace the volume of fluid lost in the vomitus, instead of dying within a few days they may live as long as three weeks although the obstruction is unrelieved.

with acute intestinal obstruction there are factors which outweigh dehydration in importance. Some degree of dehydration, however, is usually present in acute obstruction and it is often extreme. Proper attention to this factor by the administration of adequate volumes of normal salt solution before and after operation will improve the general condition of most patients and in a certain number will be a decisive factor in the outcome.

TABLE XXIV
LEVEL OF OBSTRUCTION*

Part of Bowel Obstructed	*Classification of Cases*			
	Group I†	*Group* II	*Group* III	*Total Cases*
Jejunum	7	1	0	8 (2%) }
Ileum	59	2	0	61 (18%) } 249 (74%)
Small intestine (not further specified)	53	0	127	180 (54%) }
Ileocolic intussusception	14	0	0	14 (4%) }
Large and small intestine	0	0	13	13 (4%) } 27 (8%)
Large intestine	16	29	7	52 (16%)
Not determined	7	0	0	7 (2%)
Totals	156	32	147	335

* It will be noted that in 74 per cent of the cases the point of obstruction was located in the small intestine; these obstructions were for the most part in the lower small intestine; there were only 8 cases in which the obstruction was located in the jejunum. Both the large and the small intestine were involved in 8 per cent of the cases; the large intestine alone in 16 per cent. (McIver.[5])

† Group I: All cases except those due to neoplasms or strangulated external hernias.
Group II: Obstructions due to neoplasms.
Group III: Obstructions due to strangulated external hernias.

GROUP II. Group II is composed of obstructions from neoplasms. The mortality was found to be 31 per cent. The classification of these cases on the basis of etiology and location of the obstruction is shown in Table XXV.

Obstructions from neoplasms in general do not cause interference with the mesenteric circulation and occur for the most

part in the large intestine. As would be expected, therefore, the mortality is lower than in Group I, where interference with the mesenteric circulation is common and where it is usually the small intestine that is involved. In the present series, there were 3 cases in which neoplasm directly involved the mesenteric vessels, resulting in occlusion or thrombosis with subsequent infarction of the intestine. In the late cases of obstruction of the colon, interference with the capillary circulation of the cecum, due to pressure, of sufficient extent to cause areas of necrosis or perforation, is not infrequent.

TABLE XXV
OBSTRUCTIONS FROM NEOPLASMS

Etiology and Location	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*
Obstruction from primary tumor	20	4	
Large intestine 17			
Small intestine 3			
Obstruction from metastatic tumor	6	1	
Large intestine 5			
Small intestine 1			
Obstruction presumably due to tumor*	6	5	
Large intestine 6			
Total	32	10	31

* These patients were too ill at time of entrance to the hospital to warrant any exploration. Cecostomy or colostomy only was carried out, so that the diagnosis of neoplasm was not definitely established. However, the location of the obstruction in the colon, the age of the patient and other factors led to the diagnosis of obstruction by neoplasm. (McIver.[5])

Age of the Patient. The ages of the patients with obstruction from neoplasm, in this series ranged from twenty-eight to ninety years, the average being fifty-five years. Almost 60 per cent of the patients were over sixty years of age; and postoperative complications due to this factor often entered in.

GROUP III. The mortality of Group III, comprising strangulated external hernias, as shown in Table XXVI, was 18 per cent.

Type of Hernia. By far the largest percentage of deaths was among the cases of umbilical and ventral hernia; this was also Frankau's[20] finding in his analysis of 1487 cases. These hernias are often found in fat, middle-aged individuals who are poor operative risks. There were proportionally more deaths among patients with femoral hernias than among those with inguinal hernias.

TABLE XXVI
MORTALITY IN DIFFERENT TYPES OF HERNIA*

Type of Case	*Number of Cases*	*Number of Deaths*	*Mortality (Per Cent)*
Inguinal	84 (57%)	10	12
Femoral	34 (23%)	6	18
Umbilical	18 (12%)	8	44
Ventral	9 (6%)	3	33
Epigastric	2 (2%)	0	0
Total	147	27	18

* The largest percentage of deaths in this series was among the umbilical and ventral hernias. There were proportionately more deaths among patients with femoral hernias than among those with inguinal hernias. (McIver.[5])

Duration of Symptoms before Operation. As in all types of intestinal obstruction, delay in operation increases the mortality rate. In this series of patients with obstruction from strangulated external hernia, one-half the number of deaths occurred in patients where symptoms of strangulation had existed for over twenty-four hours, as follows:

Duration of Symptoms	*Cases*	*Deaths*	*Mortality*
Less than twenty-four hours	103	13	13 per cent
More than twenty-four hours	44	13	30 per cent

Interference with the Mesenteric Circulation. All cases of strangulated hernia by definition show some interference with the mesenteric circulation. In 19 cases of the present series, as shown in Table XXVII, this was so severe and so persistent as to produce necrosis of the bowel. Eleven deaths, almost half the total number, occurred among these 19 cases. When the damaged

TABLE XXVII

CASES OF EXTERNAL STRANGULATED HERNIA SHOWING NECROSIS OF BOWEL (MCIVER[5])

Type of Case	*Portion of Bowel Obstructed*	*Duration of Symptoms*	*Type of Operation*	*Anesthetic*	*Result*
Femoral 8	Small intestine	5 days	Resection; ends brought out	Spinal procaine	R*
		7 days	Resection; ends brought out	Ether	R
		3–4 days	Resection; ends brought out	Novocaine	D*
		30 hours	Resection; end-to-end anastomosis	Ether	D
		7 days	End-to-end anastomosis	Ether	D
		2 days	End-to-end anastomosis	Apothesine spinal	R
		4 days	Inversion necrotic area and enterostomy 8 inches above repair	Novocaine	D
		8 days	Small necrotic area perforated; catheter placed in opening	Novocaine	R
Inguinal 5	Small int.	16 hours	End-to-end anastomosis	Spinal	R
		? ?	Resection; lateral anastomosis	Spinal sup. by ether	D
	Small int.	3 days	Inversion	Novocaine	R
		1 day	Gangrenous loop brought outside of peritoneum but not outside of muscle	Novocaine	R
	Trans. colon or sigmoid	4 days	Loop brought out; Mixter tube.	Novocaine	D
Umbilical 5	Small int.	4 hours	Resection; ends brought out	Ether	D
		24 hours	Resection; lateral anastomosis	Spinal	D
		5 days	Loop of bowel brought out; Mixter tube	Ethylene	D
	Small int. and trans. colon	4 days	Resection of small intestine; anastomosis	Ether	D
	Trans. colon	15 hours	Ends brought out	Ether	D
Epigastric 1	Small int.	2 days	Resection; lateral anastomosis	Novocaine	R

* R: recovered. D: died.

gut lies within the sac of an external hernia there is, perhaps, less rapid absorption of toxins than when it lies free within the abdominal cavity, as in other forms of intestinal obstruction;

but in spite of this fact, these cases showed a mortality of over 50 per cent. The existence of gangrene of the bowel of course indicates that the patient came late to operation; 11 of these patients had had symptoms for a number of days before they entered the hospital.

The portion of the bowel obstructed, the duration of the symptoms before operation and the type of operation, are also shown in Table XXVII.

Anesthetic. The operation can often be satisfactorily performed under local anesthesia. Any death following an operation for strangulated hernia, where a general anesthetic has been used, should be carefully investigated to see if the outcome could have been avoided by the use of some form of local anesthetic.

FACTORS AFFECTING MORTALITY IN ALL GROUPS. *Complications.* Shock, during operation or coming on immediately afterward, is a very common complication in serious cases. Various pulmonary complications are not infrequently encountered: bronchial pneumonia, either from the general weakened condition of the patient or from aspiration of intestinal contents, is perhaps the most common; pulmonary emboli, especially in strangulated external hernias, have been recorded.

Skill of the Surgeon and His Judgment in Selecting the Appropriate Operative Procedure. The figures from all the large public hospitals are made up from the results of a great number of different surgeons of widely varying skill and experience. This undoubtedly affects the mortality; but the factors involved are entirely too intangible to permit of any analysis.

CONCLUSION

The figures given in this chapter show the seriousness of acute intestinal obstruction. Earlier diagnosis and operation, as stressed by all writers on the subject, would unquestionably contribute to a lowering of the death rate; but the pathological condition presented by many of these cases is so serious that in

many types of obstruction the mortality is likely to continue high.

It would be desirable if in the preparation of statistics on intestinal obstruction, careful divisions of different types of cases were observed, so that it might be seen where improvement was most needed and possible. The figures so compiled would mean more than they do when they simply give the gross mortality of such a miscellaneous group as that embraced under the term "acute intestinal obstruction" and would show us in which types of cases progress is being made and in which types extra efforts are called for.

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PART III: THE CAUSE OF DEATH

Chapter XXVIII

EXPERIMENTAL METHODS

The cause of death in acute intestinal obstruction is a problem that has engaged the attention of clinicians and investigators for over a hundred years. The disease is often dramatic in the suddenness of its onset and the rapidity of its course, the patient quickly becoming extremely ill and having the general appearance and prostration associated with a profound toxemia. At autopsy the findings may not be sufficient to account for the clinical picture and death* of the patient.

The theories that have been advanced to explain the situation are numerous: the literature dealing with the experimental evidence is confused in the extreme and is filled with contradictions. Although it has been stressed by numerous investigators,[1–4] that different types of obstructions produce quite different clinical and pathological pictures, this point is still often ignored in drawing general conclusions as to the cause of death. There has also been a failure to appreciate the fact that while certain types of experimental obstruction produced in lower animals have close clinical counterparts in human cases other types have not. In considering the literature it should be realized that experimental methods have not been sufficiently

* While it is true that such situations occur, the postmortem examination will usually show some obvious morbid anatomy which is the immediate cause of death, as for example, peritonitis. The peritonitis usually comes about as a result of gross perforation of the gut or increased permeability to bacteria resulting from interference with the circulation of the bowel wall. Peritonitis may also arise as a result of operative procedures, either through leakage around intestinal sutures or from soiling of the peritoneal cavity with bowel contents at operation.

In a recent review of 123 cases autopsied following death from acute obstruction, peritonitis was listed as a principal or contributing cause of death in 66 instances. It is no wonder that in the 19th century when the condition was seen only at late operations or at autopsy, after the disease had run its full course, peritonitis (or "inflammation of the bowel") should have been considered to be always the cause of death.

The real problem is to explain the severe illness of these patients in the earlier stages of the disease, rather than to determine the immediate cause of death, which in human patients is so often some obvious complicating factor.

developed to afford a direct answer to many of the complex features of the problem. This has resulted in the endless repetition of certain types of experiments, with inconclusive or contradictory results. While indirect methods have in some instances furnished valuable information as to the cause of death, they have at times resulted in further complicating rather than clarifying the situation.

The first step is to understand clearly the fundamental types of experimental obstruction that have been employed, the results that they have produced, and their relation to clinical conditions encountered in humans.

Types of Experiments

The principal types of obstruction that have been used in experimental studies on acute intestinal obstruction are presented in diagrammatic form in Figures 57–59. There have been, of course, many minor modifications of technique.

Simple blockage of various portions of the intestinal lumen is shown in Figure 57. Hereafter, this type of obstruction will be referred to as "simple obstruction" with the qualification "small intestine—high" (Fig. 57 A), "small intestine—low" (Fig. 57 B), and "of the colon" (Fig. 57 C).

Simple High Obstruction. Experimental high obstructions (Fig. 57 A) are situated either in the duodenum or in the upper jejunum, generally within 30 to 35 cm. of the pylorus and not infrequently in the duodenum just below the entrance of the pancreatic or biliary ducts. This type of obstruction results in a very severe illness, characterized by profuse vomiting and severe dehydration. The animals soon show evidence of asthenia, apathy, muscular weakness, sometimes muscular twitchings, rapid heart rate and alterations in respiration; they not infrequently sink into coma before death intervenes. The survival period is usually between twenty-four and

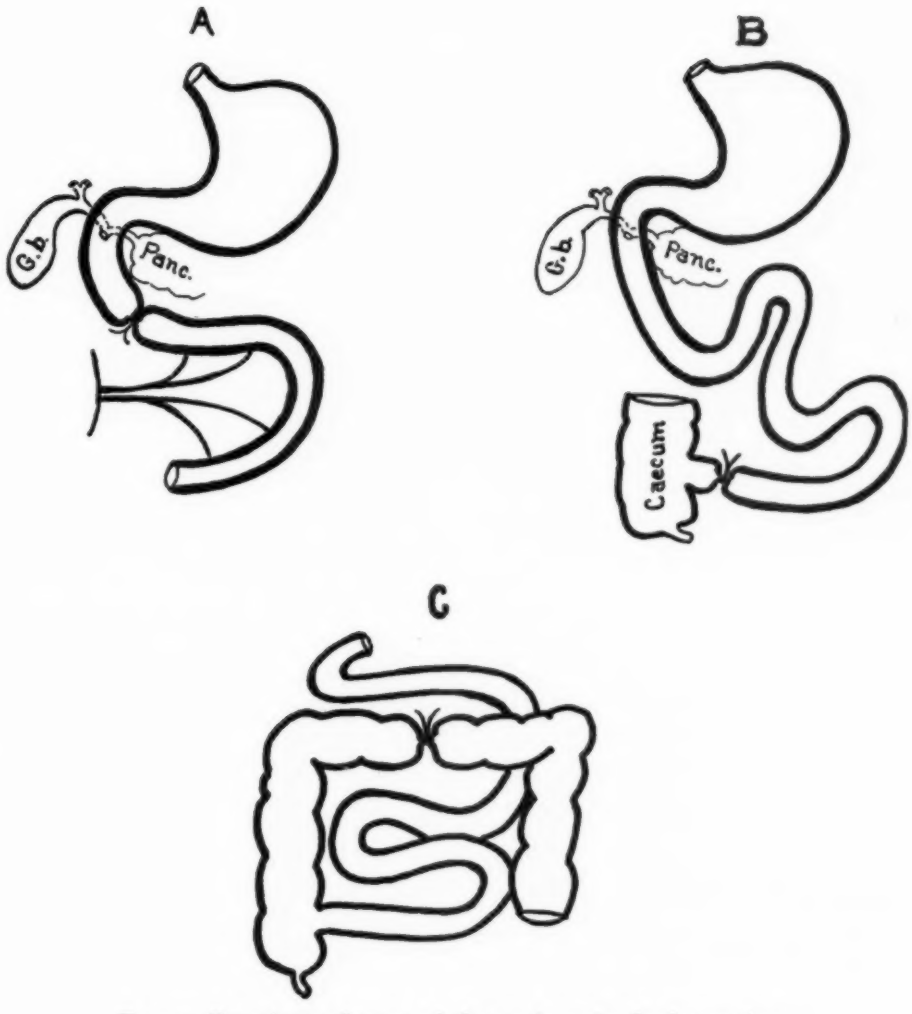

FIG. 57. Experimental types of obstruction: simple obstruction.

A. Simple blockage high in intestinal tract is a type of obstruction resulting in severe illness characterised by profuse vomiting and by severe dehydration due to loss of water and sodium and chloride ions in vomitus.

B. Simple blockage in lower ileum. Animals with this form of obstruction have a long survival period; vomiting is not likely to occur so soon or to be so profuse. This type of obstruction is less frequently used.

C. Simple obstruction of colon, a type of obstruction frequently tolerated by animals for long periods of time with few symptoms. (McIver, White and Lawson[4])

seventy-two hours,[5–7] depending largely on the distance of the obstruction from the pylorus; Draper[7] considered that if it were in any portion of the duodenum the survival period was usually under seventy-two hours and that it occurred most rapidly if obstruction was in the second portion of the duodenum.[8]

It has been a rather usual observation in experimental work on simple obstruction that the less operative damage caused to the intestine and mucosa in producing the obstruction, the less fulminating are the symptoms of obstruction that follow. Hartwell, Hoguet and Beekman[2] devised a special rubber-covered clamp that could be applied so as to produce an obstruction with a minimum amount of damage to the intestinal wall. Foster and Hausler[9] advocate section of the bowel followed by inversion of the ends. In commenting on this method they say: "Section of the intestine and inversion of the proximal and distal stumps gives a complete obstruction that is easily produced and very permanent. This technique, however, causes considerable tissue destruction and is followed by a severe constitutional reaction. The postoperative record shows that for the first five or six days, or until the inverted stumps have healed, there is a quite pronounced rise in temperature, pulse and respiration. Unless subcutaneous injections of fluid are given during this reparative period, many of the animals die. However, if the dogs survive, we have an ideal obstruction exactly comparable to that seen in human cases. The obstruction is complete, and little or no devitalized tissue is present." This statement seems to the author just the reverse of the observed clinical facts; for practically all obstructions in humans (even the simplest type) cause some local damage to the bowel at the point of obstruction, and the longer the obstruction persists, the more marked is the local inflammatory reaction. It would seem that the greater the refinements of technique in producing experimental obstructions, the less closely do they correspond with clinical cases.*

* Foster and Hausler[9] found that when they produced high obstruction by careful inversion of the ends of the intestine, and administered salt solution during the four or

Simple high obstruction has been used extensively in experimental work and has been employed by most of the investigators who have advocated the view that death in high intestinal obstruction is due to dehydration. It must be pointed out that while this experimental form is comparable to high obstructions found in clinical practice, these are relatively infrequent (see p. 158). Cases in which a kink of the jejunum occurs in the region of a recently formed gastroenterostomy, occasional instances where a band obstructs the upper jejunum or where a gallstone lodges in this portion of the intestinal tract and brings about a similar condition, are comparable, but are not often encountered; and it is well to remember this, in view of the large amount of space devoted in the literature to this type of experimental obstruction.

Simple Obstruction Low in the Small Intestine. Figure 57 B shows the type of experimental obstruction which is situated in the lower portion of the ileum.

Low obstructions have not been used so extensively in experimental work, largely because the theory of toxic absorption in the more fulminating high obstructions has monopolized the attention of investigators. Also the results of experiments in low obstruction are not so consistent as in other types. The animals, commonly dogs, usually die within from two to twelve days;[2,5,8,10,11] but sometimes they tolerate such obstructions remarkably well for surprisingly long periods. The survival periods in experiments by Hartwell et al. were five and a half days and ten days.* There is also considerable variation in the symptoms shown by the animals with this type of obstruction: the symptoms may come on promptly with profuse vomiting[2,12]; on the other hand the animals may remain well for as long as nine days[2] and die of asthenia without any marked symptoms.[1]

five days required for "the inverted raw ends of gut to heal," the treatment with salt solution could then be discontinued. The symptoms of obstruction (vomiting) ceased, the animal shows no symptoms except those which might be attributed to starvation; the survival period was over twenty days.

* Sacrificed while still in fair condition.

Thus, low experimental obstruction, although it is anatomically comparable to a large group of cases encountered clinically, namely simple obstructions of the lower ileum without strangulation, does not produce in animals a disease corresponding as closely to human cases as the disease produced by experimental high obstruction. Complete obstruction of the lower ileum in human patients, even though there be no gross interference with the mesenteric circulation, usually brings on severe symptoms: vomiting is likely to be marked and frequent and, if the obstruction is unrelieved, the survival period is not likely to exceed a few days. It is true, however, that even in humans simple low obstructions in the ileum are not so rapidly fatal as obstructions high in the small intestine.

Simple Obstruction of the Colon. Figure 57 C shows a simple obstruction of the colon. In general, the remarks made in regard to low obstruction of the ileum apply in even more marked degree to simple obstruction of the colon. Animals not infrequently tolerate this type of obstruction for long periods of time with few symptoms; the survival period is given[8,10] as from seven to fourteen days; if the obstruction is at the rectum, the survival period is about twenty-eight days.[6,8] In humans, also, simple obstructions of the colon are in general tolerated much better than obstructions in the small intestine; the clinical picture here, however, is more severe than with comparable obstructions in experimental animals, and death may be expected at an earlier date.

Closed Loop Experiments. *With Ligature of the Mesenteric Veins (Strangulations).* Figure 58 shows obstructions complicated by interference with the venous mesenteric blood supply. These obstructions are produced by the isolation of a loop of bowel with ligatures, and occlusion of the mesenteric veins* with ties. Animals operated upon in this manner

* Murphy and Vincent[1] also performed certain experiments in which they ligated both arteries and veins. They termed this "total anaemia." It rarely if ever has a clinical counterpart.

Some of the earliest experiments on strangulation were carried out by Kader.[13]

rapidly become ill and rarely survive more than twenty-four[1] to thirty[14] hours; they may die in a few hours, depending upon whether a long loop or a short loop has been used.[3,14,15]

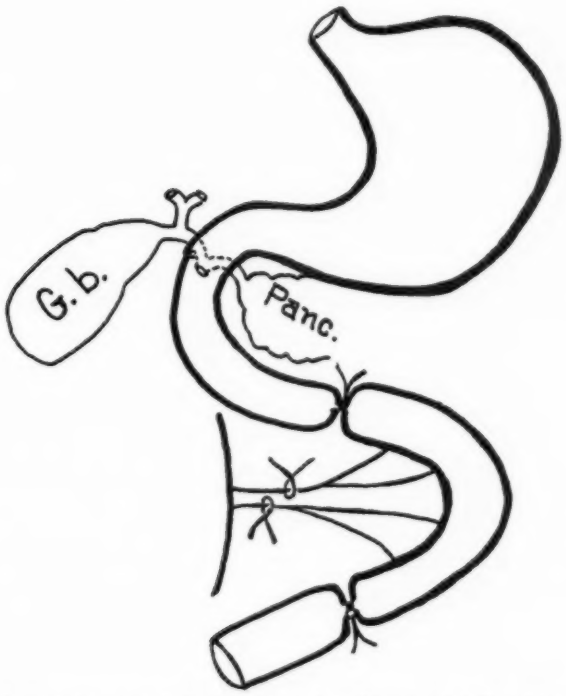

FIG. 58. Experimental types of obstruction: closed loop, with ligation of the mesenteric veins. This form of obstruction results in most serious and fulminating type of illness. Its clinical counterpart is found in cases of internal strangulation, volvulus and other types of obstruction complicated by interference with mesenteric circulation. This disease runs so rapid a course and is of such short duration that dehydration and lowering of blood chlorides do not occur to any appreciable extent. (McIver, White and Lawson [4])

The pathological picture shown by the bowel is similar to that already described in the pathology of strangulation.*

This type of obstruction corresponds closely both in pathology and in symptomatology with a type of obstruction frequently encountered clinically, namely, cases where not only a loop of bowel has become obstructed but the attached mesentery is so involved that the venous circulation is cut off.

*See May installment p. 479.

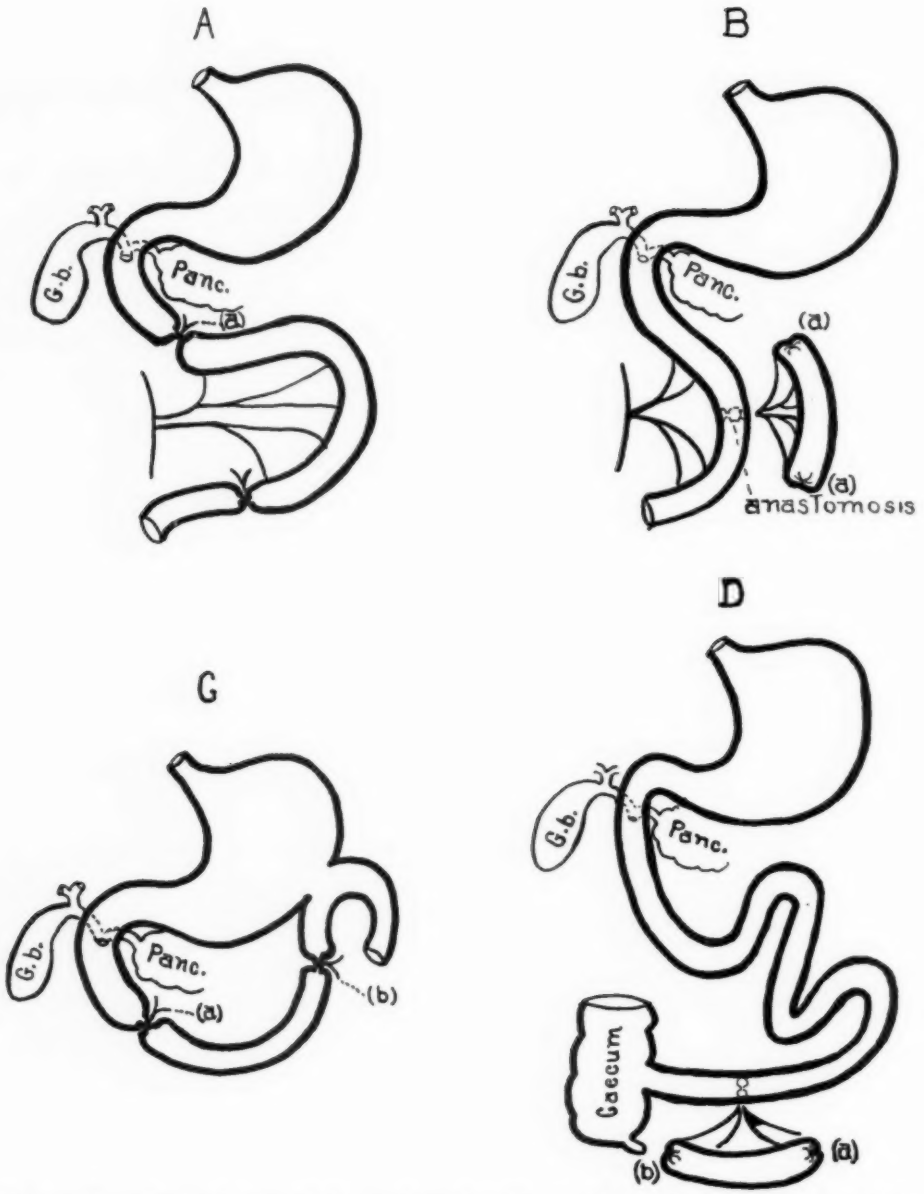

FIG. 59. Experimental types of obstruction: closed loop without ligation of the mesenteric veins.

A. Isolated loop high in intestinal tract.

B. Similar loop with continuity of intestine re-established by means of an end-to-end anastomosis.

C. Similar loop with continuity re-established by means of a posterior gastro-enterostomy (Whipple's method).

[For Remainder of Legend see p. 175.]

The seriousness of this type of obstruction as contrasted with simple obstructions has long been recognized by clinicians;[16,17] it includes strangulations with constriction of the venous supply produced by bands, by internal hernias and by volvuli; intussusceptions often come into this group, although here the amount of interference with the mesenteric circulation varies.

Closed Loop Experiments without Ligature of the Mesenteric Veins. In Figure 59 A is shown a type of obstruction that has been employed very frequently in experimental work: the isolation of a segment of the intestine by ligatures, the isolated loops usually being established in the upper portion of the intestinal tract. Frequently the continuity of the intestinal tract is restored, after isolation of the loop with its attached mesentery intact, either by an end-to-end anastomosis (Fig. 59 B), or by a posterior gastroenterostomy (Fig. 59 C). This latter procedure was largely used in the work of Whipple and his co-workers.*[18]

* In regard to the method of re-establishing the continuity of the intestinal tract by a gastroenterostomy as advocated by Whipple (Fig. 59 C), Sweet and his co-workers[19] have made the very pertinent criticism that since the gastroenterostomy may often fail to function in the presence of a ligature around the duodenum, the continuity is really not re-established. Whipple explained the fact that when he removed the lower ligature (Fig. 59 C, *b*) the animals still died although the loop was draining into the jejunum, by the assumption that a toxic secretion was formed in the mucosa of the duodenum below ligature (*a*), because this was not bathed by the normal secretions from above. As Sweet points out, however, these animals probably died because the gastroenterostomy did not function and ligature (*a*) constituted an upper intestinal obstruction. To confirm this he showed that if an isolated loop were formed as in Figure 59 B, with the additional procedure of anastomosis of one end of the loop into the jejunum, the animals lived indefinitely.

D. Isolated loop constructed low in intestinal tract, with re-establishment of continuity by an end-to-end anastomosis.

Type of obstruction represented by A, B and C produces a severe illness, survival period being usually twenty-four to forty-eight hours. Owing to profuse secretion that takes place in upper intestine, fluid accumulates rapidly, with a resulting distention and interference with circulation and nutrition of bowel wall. Perforation and peritonitis are frequent complications. Isolated loops in lower ileum (D) sometimes perforate from distention and lead to fatal results, but at other times are tolerated for a long period without symptoms. Difference in course of disease in obstructions of types A, B and C and those of type D is probably best explained on basis of more profuse secretion that takes place in upper intestine.

The survival period of animals having isolated loops in the upper portion of the intestinal tract is usually relatively short, the average length of life (according to Whipple and co-workers[18]) being 24 to 48 hours. The animals may vomit considerable amounts. Owing to the profuse secretion that takes place in the duodenum and upper jejunum, fluid accumulates rapidly in the isolated loops, with the result that there is a marked rise of pressure in the loop and consequent interference with the circulation and nutrition of the bowel wall. Perforation and resulting peritonitis are frequent complications.[20] When disintegration of the wall does not progress to this point, there are likely to be hemorrhagic areas and areas of necrosis in the mucosa.[2]

However much such experiments may have contributed to our knowledge of the general pathology following obstruction of isolated loops, it seems questionable whether high isolated loops without interference with the mesenteric circulation have any close counterpart in clinical intestinal obstruction.* Whipple and his co-workers[8] considered that such loops might be comparable to cases of volvulus where there is no interference with the mesenteric circulation. This, however, is a condition rarely found at any level in the intestinal tract, and, so far as I am aware, is unknown in the duodenum or upper jejunum. Dragstedt[20] took the opposite view and suggested that the closed loops might find a clinical parallel in types of obstruction where there is interference with the mesenteric circulation; but he pointed out that it is problematical how closely this comparison could be drawn. With his hesitation I quite agree; indeed, this experimental type of obstruction seems to me to have no close clinical counterpart, and it has perhaps diverted attention from types of obstruction that are more nearly compar-

* Wilkie[22,23] has pointed out that this type of closed loop obstruction may have a clinical counterpart in certain types of acute appendicitis: the lumen of the appendix may be blocked in its proximal end and gangrene from distention result.

It is also true that in simple low obstruction of the small intestine, kinking of distended coils may prevent free drainage back into the stomach and thus a series of semi-isolated loops may be formed resembling to some extent the experimental closed intestinal loops.

able with clinical cases. I do believe, however, that this method of study has furnished valuable information as to the changes that occur in the bowel wall when it is subjected to increased intraintestinal pressure without vent for the distending liquid either by regurgitation back into the stomach or by passing downward in the intestinal tract.

Figure 59D shows the same type of isolated loop as is shown in Figure 59B except that it is taken from the lower ileum.

Loops isolated in the lower ileum are tolerated better than comparable loops in the duodenum or jejunum. Halsted[24] in 1887 reported an experiment where the animal lived for over a month after the formation of an isolated loop in the ileum.* Von Baracz[25] also reported somewhat similar findings, which were confirmed by Whipple and co-workers.[18] On the basis of these experiments an impression is prevalent in the literature that isolated loops in the lower ileum invariably produce few if any symptoms in experimental animals. Actually, this is by no means the case, as was shown by Von Baracz's[25] early work, and also by experiments carried out by McClure[10] in which all the animals died within a few days,† not infrequently with perforation of the loop; a similar report has been made by Dragstedt et al.[20] The general statement may be made, however, that isolated loops in the upper small intestine almost always lead rapidly to fatal results; whereas in the lower intestine the loops are sometimes tolerated for long periods with very few symptoms. (See also Hartwell and Hoguet,[26] and Murphy and Brooks.[27]) This difference in the course of the disease in the two types is probably best explained by the fact that in the upper intestine the secretion is more profuse than in the lower, and consequently damage to the circulation from distention occurs more promptly.[20,27,28]

Clinically, isolated loops in the lower intestinal tract, without interference with the mesenteric circulation, may be encountered at times; but they are not frequent.

* This finding occurred during studies on various types of intestinal suture.

† The report is not definite as to the exact level of the small intestinal loops.

SUMMARY

In Table XXVIII, an attempt is made to summarize and compare the clinical and experimental findings in the major types of obstruction. It seems to be a rather universal observation in experimental work that the less damage caused to the

TABLE XXVIII

Types of Experimental Obstruction	*Clinical Observations*	*Experimental Observations*	*Clinical and Experimental Correlations*
Simple high obstruction of the small intestine (Fig. 57A)	Relatively infrequent Rapidly fatal	Most commonly used type Rapidly fatal	Comparable
Simple obstruction, low in the small intestine (Fig. 57B)	Frequently encountered Not so rapidly fatal as high obstruction	Relatively seldom employed Results variable: survival period 2 to 12 days; may have profuse vomiting or may show no symptoms for considerable periods of time	Not closely comparable
Simple obstruction of the colon (Fig. 57C)	Frequently encountered Much less fulminating course than obstruction of the small intestine	Infrequently employed Dogs may live a long time and show few symptoms	Not closely comparable
"Closed loop" with ligation of mesenteric veins (strangulation) (Fig. 58)	Very common Rapidly fatal	Frequently employed Rapidly fatal	Closely comparable
"Closed loop," high, without ligation of mesenteric veins (Fig. 59A, B, C)	Not encountered clinically	Frequently employed Rapidly fatal	Not comparable
"Closed loop," low, without ligation of mesenteric veins (Fig. 59D)	Encountered rarely, as result of operation	Infrequently used Animal often survives without symptoms	Rarely comparable

intestine and mucosa the less fulminating are the symptoms of obstruction that follow.[2,29] In human cases there is usually some gross damage to the mucosa and bowel wall at the point of obstruction.

The situation is complex and such a brief review can only hope to set forth approximately the true situation; it is hoped, however, that it may serve as a working basis for further study of the cause of death.

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[The remainder of the references to Chapter XXVIII will appear in the November issue.]

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